

ABSTRACTS

## 36th International Congress of the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) 24–27 May, 2016, Madrid, Spain

### 1. Intramuscular and intravenous e-liquid injection: a new phenomenon?

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**Objective:** Electronic cigarette design and shape have altered noticeably since their introduction to the UK market. Current e-cigarettes exist as disposable and re-chargeable devices. Cartridges of liquid nicotine solution can be placed inside these devices, or alternatively, a nicotine containing solution (known as e-liquid) can be used to replenish e-cigarette reservoirs. The solution typically contains nicotine, propylene glycol or vegetable glycerine, flavouring and water.[1] Solutions may also contain unspecified ingredients such as methyl salicylate (oil of wintergreen) [2] and nitrosamine.[1] Previous National Poisons Information Service (NPIS) data suggest that these highly concentrated, toxic liquids can be misused by means of ingestion. Recently, the NPIS has received enquiries concerning the parenteral administration of e-cigarette refill liquid. We sought to determine if the pattern of enquiries made to the UK NPIS concerning exposure to e-liquids containing nicotine is changing. **Methods:** Telephone enquiries to the NPIS between 1 April 2014 and 31 October 2015 relating to exposures concerning injections of liquid nicotine solution were examined to determine incidence and clinical features. **Results:** Of 379 enquiries identified relating to e-cigarettes and e-cigarette refill liquid, five were in relation to liquid nicotine solution administered by injection. Cases involved individuals aged 39 to 59 years. All exposures were acute. Four patients were male, 2 patients injected e-liquid intramuscularly, 1 intravenously and 2 subcutaneously. E-liquid was injected both intentionally ( $n=2$ ) and as a result of recreational abuse ( $n=2$ ). One patient, who was accidentally exposed to the solution, remained asymptomatic. Three patients developed mild features including a localised skin reaction, somnolence, fever and palpitations. This corresponded to a maximum poisons severity score (PSS) [3] of one. Chest pain and QT prolongation occurred in one case resulting in a maximum PSS score of two. **Conclusion:** Parenteral use of e-liquid, including recreational use, is occasionally encountered. Although local problems such as extravasation injury, skin necrosis and compartment syndrome may be expected after injection of this agent, as nicotine is extremely irritating to tissues, serious outcomes were not encountered in this small case series.

### References

- [1] Wollscheid KA, Kremzner ME. Electronic cigarettes: safety concerns and regulatory issues. *Am J Health Syst Pharm.* 2009;66:1740–1742.
- [2] Bassett RA, Osterhoudt K, Brabazon T. Nicotine poisoning in an infant. *N Engl J Med.* 2014;370:2249–50.
- [3] Persson H, Sjöberg G, Haines J, et al. Poisoning Severity Score: Grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998; 36:205–13.

### 2. Fatal outcome after suicidal subcutaneous injection of E-cigarette liquid

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**Objective:** The use of electronic cigarettes is a growing trend worldwide as well as in Finland. Easy access and high nicotine concentration make these products a potent health hazard. Accidental or intentional misuse of e-cigarette liquids can lead to severe poisonings or even death. Nicotine poisonings are well known, however, there are only few case reports in the literature with serious poisonings involving e-cigarettes. We describe a case of intentional subcutaneous injection with fatal outcome. **Case report:** A 29-year-old woman with a history of severe depression called an ambulance after admittedly taking 75 mg of diazepam and subcutaneously injecting 10 ml of e-cigarette liquid bought from the Internet (unknown strength, liquids usually contain 10–40 mg/mL of nicotine) into her abdomen. On arrival at the emergency ward 1 hour after injection she was very agitated, hysterical, hyperventilating continuously and mildly tachycardic. Otherwise her vital signs were unremarkable. She was given 30 mg oxazepam orally to help calm her. Two hours after the injection she became drowsy and had a seizure followed by asystole. Prompt cardiopulmonary resuscitation resulted in return of spontaneous circulation (ROSC 12+2 minutes). The patient was intubated and transferred to the ICU. After initial stabilization she was hypertensive, tachycardic, lactatemic and developed respiratory acidosis. She had also aspirated the activated charcoal which had been given in the ambulance. Symptomatic treatment with fluids, norepinephrine and cefuroxime was continued. Her pupils remained dilated and unresponsive to light. All sedatives were discontinued in hope of recovery of consciousness. Muscle tremors were treated with clonidine, pethidine and levetiracetam without response. Her level of consciousness (Glasgow Coma Scale 3) remained unchanged during follow up. Initial brain computerised tomography (CT) scan showed diffuse parenchymal swelling. Brain death and cessation of cerebral blood flow was confirmed by neurological examination, and CT angiography 35 hours after hospital admission. As the patient had previously been somatically

healthy and was not known to have objected, the patient was considered a potential organ donor. The kidneys were subsequently used successfully for organ transplantation without any specific problems related to the intoxication known to date. **Conclusion:** E-cigarette liquids are potentially fatal if misused. Our case further supports this opinion.

### 3. Household product safety evaluation over a 15-year period based on systematic follow up

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**Objective:** To evaluate the safety of household products by analyzing unintentional human exposures to household products (UHEHP) over the past 15 years. **Methods:** The Lille Poison Centre (LPC) routinely follows all human cases throughout the year whatever the origin of call, source of exposure, type of patient, severity of symptoms or decisions taken during the initial call. The follow up is done by telephone for cases left at home by contacting the patient or their family and by telephone and letter to the physician if the patient is hospitalized. Symptoms reported during the initial call and follow up are collected in the case database CIGUE (CDC) and the severity is evaluated using the Poison Severity Score (PSS). If after two attempts, no response is obtained, the case is classified as "lost to follow up" and evolution as "unknown". Cases are followed until recovery even on a long-term if needed. All UHEHP cases (2000–2014) were extracted from the LPC CDC. Data analysis concerned: type of patient (adult, child), presence of symptoms at initial call and follow up, known follow up, evolution (recovery, death) and severity of symptoms (PSS1, PSS2, PSS3).[1] **Results:** From 2000 to 2014, there were 199,194 cases collected by the LPC; of these 97,545 cases (49%) were related to UHEHP. Most cases involved children (73%). During the initial call the LPC staff advised patients to attend hospital in 23% of cases (22,426) or advised them to stay at home in 77% (75,119). All 97,545 cases were contacted for follow up and complete follow up was obtained for 78,123 cases (80%). Among them, 11 patients died, 137 (0.2%) developed symptoms of severe severity (PSS3), 1259 (1.6%) of moderate severity (PSS2), 31,099 (40%) of low severity (PSS1) and 45,614 (58%) remained asymptomatic. **Conclusion:** Without systematic follow up, the true consequences of UHEHP cannot be appreciated and unsuspected severity at the initial call may be missed.

#### Reference

- [1] Persson H, Sjöberg G, Haines J, et al. Poisoning Severity Score. Grading of acute poisoning. *J Toxicol Clin Toxicol*. 1998;36:205–213.

### 4. MAGAM II DISC: eye exposures caused by cleaning products in Denmark, Italy, Slovakia and Czech Republic

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**Objective:** Local effects following cleaning product eye exposures are frequently reported to European poisons centres. The objective of this study is to quantify the risk of irreversible eye damage caused by exposure to detergents and cleaning products based on human exposure data from European poison centres (PC). **Methods:** From June 2013 to February 2015 PCs of Denmark, Italy, Slovakia and Czech Republic (DISC) recorded and followed up all human eye exposures to detergents or maintenance products in a harmonised manner (including telephone interviews and collection of medical reports). Poisoning severity grading was performed according to PSS. **Results:** In total details on 657 exposures were collected and analysed (338 children <14 years, 2 adolescent <17 years, 311 adults, 8 unknown age; 341 females, 310 males, 5 unknown gender). All exposures were accidental, including 13 occupational; 6% of exposures involved products for professional use. Follow up was successful for 598 cases (91%), and 5 cases had incomplete follow up; 30 ophthalmologists' written reports (5%), 14 other written medical reports (2.3%) and 3 medical reports transmitted by a layperson (0.5%) were obtained. Severity of injury was classified as minor in 483/598 cases (81%) with completed follow up, 71 as moderate (12%), 2 as severe (0.3%) while 59 cases could not be graded based on the data collected. Frequent symptoms notified were signs of irritation. Eye irrigation was performed in 95% of cases. In 17% of cases symptoms lasted more than 24 hours (minor 8%; moderate 8%; severe 0.3%). Healing was reported in 86%, with healing expected in another 8%. Two cases with residual eye damage after 21 days were recorded: a child suffered from persistent sensitivity to light, a female had photophobia and reduced vision. **Conclusion:** Most patients with ocular exposure to cleaning products had minor symptoms and were treated with eye irrigation. Healing within hours or days was reported in most cases but two patients suffered from residual eye symptoms after 20 days. This is in contrast to results of the MAGAM II Study [1] based on reports from Germany and Austria, where no cases with residual damage after 20 days were recorded. **Acknowledgements:** Financing by the AISE (International Association for Soaps, Detergents and Maintenance Products) in Brussels covers the running costs of the study. The fund provider has no influence on the research work.

#### Reference

- [1] Hermanns-Clausen M, Desel H, Färber E, et al. MAGAM II: Prospective observational multicentre poisons centre study on eye exposures caused by cleaning products. *Clin Toxicol (Phila)*. 2015;53:315–316.

## 5. Evaluation of medical outcomes associated with exposures to liquid laundry detergent packets reported to the US National Poison Data System

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**Objective:** Since becoming available in the US in 2012, the popularity of liquid laundry detergent packets (LDPs) has increased. Along with growing popularity and availability, reported exposures to LDPs to US Poison Centers (PCs) have also increased. The National Poison Data System (NPDS) captures data from these reports and provides a near real-time snapshot of exposures reported in the US at any time. This analysis serves to describe LDP exposures reported to US PCs via the NPDS, with focus on medical outcomes associated with these exposures. **Methods:** The NPDS was searched for exposures involving 1 or more LDP products (no other substances) from 1 January 2013 through 30 June 2014. Only cases followed to known outcome were included to facilitate analysis of the most detailed records. Descriptive statistics were used to describe demographics, exposure characteristics, and outcome-related variables. **Results:** During the study period 17,857 exposures to LDPs were reported, of which 13,307 (74.5%) were followed to a known outcome and involved only a LDP. The slight majority of cases involved male patients (51.3%;  $n = 6825$ ). Most exposures occurred in children aged <6 years (93.9%;  $n = 12,497$ ), with the highest incidence in children aged 2–4 years (42.9%;  $n = 5704$ ). Treatment in a healthcare facility (HCF) was recommended or received in 51.7% ( $n = 6876$ ) of cases with 11.3% ( $n = 778$ ) of those involving HCF admission. Most cases involved a minor effect (66.0%;  $n = 8781$ ) or no effect (22.6%;  $n = 3002$ ), but 4 deaths (<0.1%) were reported. All deaths involved unintentional exposure reasons, but demographic and exposure characteristics were otherwise dissimilar. Two deaths involved children (ages 7 and 18 months) and 2 involved adults (ages 72 and >89 years). The route of exposure was ingestion in all 4 cases, with aspiration reported in both adults. Causality information was only available for the fatality involving the 7 month old; the LDP exposure was determined to be undoubtedly responsible for the outcome. **Conclusion:** NPDS data can be used to evaluate risks associated with new household products and allow federal agencies to educate the public and improve product safety. Recent packaging changes and warning labels to deter unintended exposures have been implemented although the effectiveness of these changes has yet to be systematically evaluated. With further labeling and packaging standards designed to limit ingestions of LDPs pending, ongoing evaluation of NPDS data will be useful in monitoring exposure to these products.

## 6. Accidental childhood exposures to single use laundry detergent packs: 3-year analysis of an on-going prospective study

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**Objective:** Prior to introduction of single-use liquid laundry detergent (LLD) packs in North America (February 2012), a prospective observational study was initiated among 12 US Poison Control Centers (PCCs) to evaluate the reporting rates, situational variables and biological response to this product category. **Methods:** An analysis of LLD pack exposures involving children (age  $\leq 5$  years) reported during the first three years of peak market experience, July 2012 through June 2015, using data from PCCs participating in the ongoing prospective study (serving 25% of US population). The complete PCC record was obtained to evaluate key parameters including demographics, morbidity and exposure scenario. The case narrative was reviewed to verify coding accuracy and to isolate situational and packaging characteristics associated with each exposure. Trend analysis was performed and normalized using Nielsen consumption data. **Results:** There were 8520 childhood exposures (age  $\leq 5$  years) reported during the three year period. Children age  $\leq 3$  years represented 90.7% ( $n = 7730$ ) of all cases, and ingestion (84%) and ocular (14%) were the major routes of exposure. The total case count was similar for Year 1 ( $n = 2723$ ) and Year 2 ( $n = 2718$ ), however increased in Year 3 ( $n = 3079$ ) due to the introduction of new products. Moderate/major outcome represented 10.2%, 7.6% and 6.5% of total cases in Y1, Y2 and Y3 respectively. Review of evaluable case narratives ( $n = 3145$ ) indicated that exposures were more likely to be facilitated by another adult/child for children age <1 year (16.9%) versus older children (9.3%). Among children who accessed the LLD pack directly, 38.5% accessed the product outside of the original packaging. Exposure frequency was lowest when the LLD pack was accessed from a location that was out of sight and out of reach (3.6%) versus out of reach alone (17.9%). In total 68.7% of exposures involved access from a location that was within sight and within reach. Among cases with a specific product coded ( $n = 8144$ , 95.6%), multi-colored products did not demonstrate a disproportionately higher rate of exposure. Additionally, the exposure rate per 100,000 units purchased peaked in May 2013 for the market leader (P&G), followed by a sustained reduction that coincided with the timing of packaging changes and implementation of educational initiatives. **Conclusion:** Childhood exposure to LLD packs continues to be an important focus of US PCCs. Data for the market leader demonstrated a reduction in exposure rates, which coincided with the implementation of prevention strategies.

## 7. Paediatric eye exposures to household products

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**Objective:** Ocular exposure to household products in children is a public health event. The risk of corneal damage due to accidental exposure to liquid laundry detergents capsules (LLDC) has been documented [1] and we sought to examine ocular exposure to household products reported to the Milan Poison Centre. **Methods:** We analyzed our paediatric eye exposures from 1 March 2014 to 28 February 2015. The type of data collected included: child identification, call site, route of exposure, dose value and unit, agent name, active ingredients, category code, field of application, packaging, product diluted, eye exposition, circumstances of exposure, impacted eye, symptoms present,

therapy, medical assessment, symptom duration, outcome, degree of severity according to the Poison Severity Score (PSS). **Results:** During the study period 247 paediatric eye exposures were reported. The age group distribution was infants ( $n=8$ ), school-children ( $n=16$ ) and toddlers ( $n=223$ ), involving 157 males and 90 females. Of these, 150 children were taken to hospital, 86 stayed at home and 12 were unknown. The category code distribution involved: all purpose and neutral cleaners ( $n=71$ ), laundry detergents ( $n=49$ ), unknown ( $n=28$ ), textile bleaches ( $n=25$ ), glass cleaners ( $n=15$ ), dishwashing detergents ( $n=13$ ), bathroom cleaners ( $n=10$ ), cleaners not specified ( $n=4$ ) and others ( $n=32$ ). The circumstances of exposure were: children sprayed the product in the face ( $n=61$ ), squeezing a liquid detergent capsule (LDC) that leaked ( $n=31$ ), playing with the product ( $n=10$ ) and biting the LDC ( $n=6$ ). Clinical effects included inflammation ( $n=47$ ), irritation ( $n=40$ ), lacrimation ( $n=21$ ), severe pain ( $n=19$ ), mild palpebral oedema ( $n=11$ ), irritation ( $n=9$ ), corneal abrasion ( $n=7$ ), conjunctivitis ( $n=7$ ); photophobia ( $n=6$ ), aggravated conjunctivitis ( $n=3$ ), purulent conjunctivitis ( $n=1$ ), impaired vision ( $n=1$ ), mild sensation of foreign body ( $n=1$ ) and marginal corneal ulcers ( $n=1$ ). Irrigation was performed in all cases. No symptoms were present in 29 cases; minor symptoms were present in 183 cases and moderate symptoms in 18 cases. Cases with symptom duration more than 24 hours were minor ( $n=4$ ) or moderate ( $n=10$ ). PSS was not assignable in 17 cases. Full recovery was reported in 182 cases with healing expected in 19 cases. **Conclusion:** No severe cases were reported. LLDCs were involved in 4 cases of corneal abrasion. One child with eye exposure to a LDC described yellow vision for few minutes and one child exposed to an oven and grill cleaner had a corneal ulcer that healed rapidly.

## Reference

- [1] Whitney RE, Baum CR, Aronson PL. Diffuse corneal abrasion after ocular exposure to laundry detergent pod. *Pediatr Emerg Care*. 2015;31:127–128.

## 8. Rate estimates and trends of pediatric exposures to liquid laundry detergent capsules in Italy

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**Objective:** In Italy, liquid laundry detergents capsules (LLDCs) were initially launched in August 2010. Immediately after, the National Poison Control Centre in Milan (NPCCM) documented an increased number of incidents involving young children [1] and different preventive actions had been undertaken by industry, including precautionary statements on outer packaging and television advertisements, and information campaigns (since January 2011), changes of the lid of outer packaging (in February 2012), and opaque outer packaging (in August 2012). In the present study, LLDC exposure rates during a five year period are reported. These measures are proposed as a basis for evaluating the impact of these preventive measures. **Methods:** The database of NPCCM was searched to identify all cases of exposure to laundry detergents between 1 September 2010 and 31 December 2014 in

children aged <5 years. The quantity of LLDCs sold by month and company, i.e. a major company (MC-LLDCs) and other companies (OCs-LLDCs) was used to calculate exposure rates, i.e. number of cases exposed to LLDCs/millions of units sold/month by year and company. Changes in exposure rates were identified using change-point analysis. A change was considered significant when the confidence interval (CI) was 95% or higher, as estimated by bootstrapping techniques. The mean numbers of cases of exposure to MC-LLDCs and OCs-LLDCs/month observed in the identified pre- and post-change point periods, adjusted by quantity sold, were compared using analyses of variance (ANOVA). **Results:** There were 1041 patients exposed to MC-LLDCs and 511 to OCs-LLDCs. The average rate of MC-LLDCs exposures changed abruptly in December 2012 (CI for change: 100%), four months after the introduction of opaque outer packaging: in September 2010–November 2012 (pre-change point period) the average rate was 1.9 cases/million units sold, while in December 2012–December 2014 (post-change period) it was 0.9 cases/million units sold. No significant changes were observed for rates of exposure to OCs-LLDCs (average rate 1.0 cases/million units sold). The ANOVA analysis indicated that in the post-change period there was a statistically significant reduction in the mean number of cases exposed to MC-LLDCs, accounting for –19.6 cases/month (95% CI: –23.2 to –16.1,  $p < 0.0001$ ). **Conclusion:** These observations indicate that reducing visibility of LLDCs can lower exposure rates by 50%. According to the present data, precautionary statements and informative campaigns had no impact when products were sold in transparent outer packaging.

## Reference

- [1] Celentano A, Sesana F, Settini L, et al. Accidental exposures to liquid detergent capsules. *Clin Toxicol (Phila)*. 2012;50:353.

## 9. Liquid detergent capsules: how to make the product and its use safer

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**Objective:** In the Netherlands the number of accidental exposures to liquid detergent capsules (LDCs) is increasing. As exposure to laundry LDCs more often results in more serious effects than exposure to traditional laundry detergent products, information about the circumstances of exposure is valuable for developing preventive measures. The Dutch Poisons Information Center participated in a follow up study of the International Association for Soaps, Detergents and Maintenance Products (AISE), studying the circumstances of exposure to all LDCs. **Methods:** In the study period from 1 October 2014 to 31 March 2015, all cases of exposure to LDCs used for laundry, automatic dishwashing or other cleaning purposes, were prospectively followed up. A standardized questionnaire was used to interview the parents (of children <16 years) or the patients. The study protocol was approved by the medical ethics committee. **Results:** In total 148 cases met the inclusion criteria and 101 could be followed up, almost all involved children (average age 2.7 years). Cases concerned 84 laundry, 12 automatic dishwashing and 5 general cleaning products. Ingestion was the predominant route of exposure (94%). Symptoms occurred in 82% of patients (66% minor, 16% moderate effects). Vomiting was reported in 54% of patients after ingestion. The occurrence of vomiting increases the risk of aspiration

and chemical pneumonia. However, chemical pneumonia was not reported. Most of the incidents happened at home. In 41% of the cases the child took the LDC from the closed original packaging. Only 12% of the boxes were stored in a high cabinet at that time. In 12% the LDC was ready for use and found by the child on top of or inside the (dish)washing machine. In 7% parents gave the capsule to the child to play with or to help while doing the laundry. In 8% of cases the capsules were lost by the parents and found by the child. **Conclusion:** An important aspect of accidental exposures to LDCs is their appearance. One third of the interviewed parents suggested a change to the appearance of LDCs to diminish their attractiveness to children. As many children took a LDC from the closed original packaging, the current packaging is clearly not very child resistant. Improving the child safety for storage boxes might help to reduce the number of childhood exposures. Continuing education of parents with a focus on how to store these products and keep them out of sight and out of reach of children, as well as raising awareness about the potential health risks, remains important.

## 10. Hot-cold packs: trifle or threat?

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**Objective:** Oral ingestions of hot/cold gels are challenging in product identification and risk evaluation. A single case of severe intoxication has been reported.[1] We analysed cases reported to the Poisons Centre (PC). **Methods:** A retrospective analysis (January 1995 to June 2015) of the PC database (search terms: cool pack, hot/cold compress and comparable product names). Cases involving multiple agents were excluded. **Results:** In total 787 cases of oral gel exposure (0.17% of all human PC cases) were retrieved; 781 mono-ingestions (99%) with a follow up rate of 30% ( $n=235$ ) were analyzed. Most cases were accidental (777, 99.5%); 3 were suicidal and 1 with unknown circumstance. The majority of patients were infants (73%). Most children ingested small amounts compared to the elderly who predominantly ingested a larger quantity. Initially ( $n=781$ ) 93.5% of patients were asymptomatic, 6.1% with minor and 2 patients with moderate symptoms. For patients with follow up ( $n=235$ ) most remained asymptomatic (86.4%); 13% had minor and 2 had moderate symptoms. There were no severe cases. Symptoms ( $n=47$ ) were mostly gastrointestinal (79%) and non-specific (72%). There was one case of dyspnoea without causality and one report of pronounced acidosis. Of the cases with follow up 99.1% made a full recovery (0.9% unknown). The patient with acidosis was an elderly patient with dementia who ingested one whole hot cold pack (unknown ingredients). Acidosis occurred after 6–8 hours (pH 7.174 minimum, base excess maximum -16.7). Repetitive infusions of sodium bicarbonate and ethanol therapy (started after 21 hours) were given. No ethylene glycol was detected and there was no crystalluria. The patient recovered fully. In total 116 different names were documented, with the product name identified in 28%; the ingredients were determined in 36% of identified products. None of these contained ethylene glycol. **Conclusion:** No severe intoxications were identified. Nevertheless, infants are at risk if the product contains glycols or ammonium nitrate. There is one report of renal failure in a child after ingestion of hot/cold gel in Australia.[1] Many different and poorly labelled products are available. Though most patients had mild or no symptoms, one developed pronounced acidosis. Correlation of ingestion and symptoms is probable, even without detection of a toxic agent. Therefore a global all-clear is not possible. Obligatory labelling would simplify risk evaluation. Further investigations could detect

severe symptomatic cases to underline the need for reliable labelling of ingredients.

## Reference

- [1] [cited 2015 Nov 12] [http://www.bfarm.de/SharedDocs/Risikoinformationen/Medizinprodukte/DE/anwendungsempfehlung\\_Kalt-WarmKompressen.html](http://www.bfarm.de/SharedDocs/Risikoinformationen/Medizinprodukte/DE/anwendungsempfehlung_Kalt-WarmKompressen.html) [Website in German].

## 11. Toxicity resulting from automotive screenwash exposures reported to the UK's National Poisons Information Service from 2012 to 2014

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**Objective:** Automotive screenwashes may contain ethylene glycol, and/or methanol and/or isopropanol, or ethanol alone or in combination with the other ingredients. The concentrations and combinations of each constituent can vary considerably between products. Some products are sold “ready-to-use” off the shelf while others require dilution in water at various ratios dependent on season. This study investigated the toxicity resulting from exposure as reported to the UK's National Poisons Information Service by doctors and other healthcare workers. **Methods:** Enquiries were analysed retrospectively for the 3 year period January 2012 to December 2014. **Results:** There were 208 enquiries involving 181 exposures. The majority of exposures followed ingestion ( $n=171$ , 94%), 6 of which also involved skin contact. The remainder were due to dermal exposure alone ( $n=4$ ), eye exposure alone ( $n=2$ ), inhalation alone ( $n=2$ ), exposure to the ear ( $n=1$ ) and multiple routes ( $n=1$ ). Of those exposed 24% were children below 5 years of age and 37% were under 18 years of age. The composition of the screenwash ingested was known with certainty in only 99 cases. Of these 27 of the ingested screenwashes contained methanol alone, 36 were combined with isopropanol, 14 with ethylene glycol and 6 with ethylene glycol and isopropanol. In addition, 7 screenwashes contained ethylene glycol alone, 3 contained isopropanol, 4 contained ethanol alone and 2 contained other ingredients. Ethanol was present in 71% of 90 methanol or ethylene glycol containing products and 82% of 45 products containing isopropanol. Most patients who ingested screenwash were asymptomatic ( $n=126$ ), but 36 developed minor features (PSS 1), 3 developed moderate features (PSS 2) and one elderly man developed severe features (PSS 3) and later died after having ingested screenwash containing ethylene glycol and an iron-containing fertiliser. Abdominal pain ( $n=7$ ), nausea ( $n=6$ ), vomiting ( $n=6$ ), metabolic acidosis ( $n=6$ ), headache ( $n=5$ ), somnolence ( $n=5$ ) and raised osmolar gap ( $n=2$ ) were reported most commonly after ingestion. **Conclusion:** Most patients ingesting automotive screenwash did not develop the anticipated features of toxicity. The implication is that the amount of screenwash ingested was very small or that the presence of ethanol (present in 71% of products) protected against potential toxicity from methanol and ethylene glycol-containing products. Ethanol was present in 82% of products containing isopropanol ( $n=45$ ) and may have increased toxicity.

## 12. Eucalyptus oil poisoning in Australia: do we need koala-proof packaging?

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**Objective:** Eucalyptus oil is a popular household product in Australia. It is an essential oil marketed as a discrete product but is also found in inhalant solutions (including vaporiser fluids), topical preparations and cleaning products. Ingestion of as little as 5 mL of concentrated oil can cause toxicity in children. This study aimed to describe cases of eucalyptus oil exposures reported to Australia's largest poisons centre over an 11 year period. **Methods:** The New South Wales Poisons Information Centre (NSWPIC) receives approximately 100,000 calls per year from healthcare professionals and the general public. The NSWPIC database was retrospectively searched for exposures to eucalyptus oil from 1 January 2004 to 31 December 2014. **Results:** Over the 11-year study period there were 6085 unique exposures to eucalyptus oil reported to the NSWPIC. Of these, 77% ( $n=4847$ ) were accidental, 15% (903) were therapeutic errors, and 5% ( $n=273$ ) were intentional. The vast majority (87%  $n=5294$ ) involved ingestion. At least 792 cases were reported ingestions of  $\geq 5$  mL, 239 ingested  $\geq 20$  mL, and 53 had reportedly ingested  $\geq 100$  mL. Most patients (57%,  $n=3452$ ) were aged 0–14 years, 33% ( $n=1982$ ) were aged 14–74 years, 4% were aged 75 years and over. Patients were treated in hospital in 20% ( $n=1253$ ) of cases. Overall 28% ( $n=1714$ ) of patients were symptomatic at the time of call. Clinical features reported included vomiting, ataxia, seizures, miosis, sedation, hyperactivity, respiratory depression requiring intubation, and aspiration pneumonitis. In addition to these 6085 exposures, there was a further 5334 records of exposure to vaporiser fluid combinations, which typically contain eucalyptus oil at various concentrations. **Conclusion:** This study summarises a large number of cases of eucalyptus oil exposure reported to the NSWPIC. This is a relatively common enquiry, and although small ingestions can often be managed at home, one fifth of exposures required hospitalisation. Common reasons for ingestion include children accessing the product from a vaporiser unit or directly from the bottle; or administration of eucalyptus oil in error for medication. Given the frequency of these exposures and the potential toxicity, more preventative measures are needed to improve product safety. In Australia, eucalyptus oil does not need to be in child-resistant packaging if in a container of  $\leq 15$  mL. Given that toxicity can result at doses lower than this, this rule seems inadequate. Further preventative measures could include changing packaging to reduce the likelihood of therapeutic errors, and re-design of vaporiser wells.

## 13. Surveillance of pediatric exposure to laundry detergents: comparison between cases exposed to liquid capsules and traditional products

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**Objective:** Previous investigations have shown that liquid laundry detergent capsules (LLDCs) have the potential to cause corrosive eye damage, pulmonary toxicity and serious laryngopharyngeal injuries in young children.[1] The present paper is aimed at providing a comparison between the main characteristics of cases exposed to LLDCs and traditional laundry detergents (TLDs) and a measure of the effect of LLDCs exposure as a risk factor for moderate/high severity. **Methods:** The database of the Italian National Poison Control Centre in Milan was searched to identify all cases of unintentional exposure to laundry detergents in children aged  $< 5$  years between 1 September 2010 and 31 December 2014. Severity of poisoning was classified according to the Poisoning Severity Score.[2] Cases of exposure to LLDCs and TLDs were compared by means of Pearson's  $\chi^2$  test or Fisher's exact test. A logistic regression model was used to measure the strength of the associations between different types of laundry detergents and severity of poisoning by maximum likelihood estimate of the odds ratios (ORs) and the related 95% confidence intervals (CIs), adjusted by exposure period. **Results:** A total of 2748 cases were identified; 1551 (56%) LLDCs exposures and 1042 (38%) TLDs exposures, including 719 (26%) cases involving liquids, 275 (10%) granules, and 48 tablets (2%). In comparison to patients exposed to TLDs, those exposed to LLDCs were characterized by a predominance of cases treated in hospital (69% versus 41%,  $p < 0.001$ ), suffering clinical effects (75% versus 21%,  $p < 0.001$ ), exposed via multiple routes (12% versus 6%,  $p < 0.001$ ), and presenting with moderate/severe poisoning (10% versus  $< 1\%$ ,  $p < 0.0001$ ). Seven cases exposed to LLDCs developed severe poisoning. Among symptomatic cases, those exposed to LLDCs more frequently developed gastrointestinal (76% versus 69%,  $p < 0.05$ ) oropharyngeal (27% versus 12%,  $p < 0.001$ ) and respiratory (19% versus 11%,  $p < 0.01$ ) effects in comparison to those exposed to TLDs. The OR estimate showed that the risk of moderate/severe poisoning was 21.5 times higher in children exposed to LLDCs of one major company (OR 21.5; 95% CI 5.3–88.0) and 12 times higher if exposed to LLDCs of other companies (OR 12.0; 95% CI 2.8–50.7). **Conclusion:** These observations underscore the need to prevent hazardous exposure LLDCs and to reduce their intrinsic toxicity.

## References

- [1] Forrester MB. Comparison of pediatric exposures to concentrated "pack" and traditional laundry detergents. *Pediatr Emerg Care.* 2013;29:482–486.
- [2] Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998;36:205–213.

## 14. Acute and chronic oesophageal injury following caustic ingestions in a 25-year cohort

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**Objective:** Caustic ingestions can cause life-threatening injuries within hours. In survivors with significant oesophageal injury there is a risk of oesophageal stricture but the incidence and risk factors are unclear. This study aimed to determine the incidence of

oesophageal strictures in caustic ingestions and potential risk factors. **Methods:** All exposures to caustic substances (acids, alkalis and other corrosives) were identified from a 25 year database of poisonings. Cases involving caustic ingestion were included. All patients at least one year post-ingestion were followed up. Chart review was completed from hospital records and patients were interviewed by telephone (up to 5 attempts), including a Mayo dysphagia questionnaire. The primary outcome was confirmed oesophageal stricture. Other outcomes included in-hospital mortality, subsequent mortality, inpatient endoscopy results and length of stay (LOS). **Results:** From 120 exposures 31 involved other routes, leaving 89 caustic ingestions in 88 patients. The 88 patients had a median age of 31 years (1–87 years) and 42 (48%) were male. There were 13 cases involving strong alkalis (pH >12), 8 strong acids (pH <2), 29 domestic bleaches, 30 other domestic products, 6 non-domestic products and three unknown substances. One patient developed a tracheoesophageal fistula (3B injury), treated with a colonic conduit. Another developed a stricture, which was diagnosed 25 days following 2A injury and was dilated endoscopically. Both these patients developed strictures after ingestion of a strong alkali. Median LOS was 1 day (0–66). Inpatient endoscopies were performed in 29 patients: 5 normal, 5 grade 1, 16 grade 2 and 3 grade 3. Of 88 patients, 12 died (3 inpatients died within 24 hours [phenol, sodium azide, hydrochloric acid], 9 subsequently from unrelated causes), 28 could not be contacted (one had two ingestions during the study period; 2 had normal oesophageal investigations within a month) and 48 were contacted (1.7–24 years later). Of the 48 patients 41 were interviewed. Four reported dysphagia on the questionnaire; one had normal endoscopy, one awaits endoscopy, one was psychotic and one choked on fluids but not solids. Five could not be interviewed (normal endoscopy [1], no dysphagia per carer [3] and stroke [1]). **Conclusion:** In a Western country there was a broad mixture of caustic substances ingested. Although there were a number of deaths and severe complications, these were apparent within hours, and occurred with highly caustic substances. Only one delayed stricture occurred and this was not predicted by inpatient endoscopy.

## 15. A review of the toxicity of picaridin-containing insect repellents reported to the National Poison Data System

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**Objective:** The insect repellent picaridin, available in Europe since 2001 and the US since 2005, is reported to be of low toxicity. The purpose of this study was to review poison center data regarding ingestion of insect repellents containing picaridin and compare those to insect repellents containing diethyltoluamide (DEET) and other non-DEET-containing insect repellents through the National Poison Data System (NPDS). **Methods:** The NPDS was queried for all human exposure cases reported to US poison centers involving single agent ingestions of insect repellents (both intentional and unintentional) between 2000 and 2014. Records were retrieved using the American Association of Poison Control Center generic categories 201048 (Insect Repellents with DEET) and 201049 (Insect Repellents without DEET). A subset of picaridin exposures were assessed using Poisindex<sup>®</sup> product ID 6744589. Insect repellents of unknown type were not included in this analysis.

Data analyzed included demographic, exposure characteristics, clinical effects, and medical management of these exposures. **Results:** There were 67,927 insect repellent exposures reported, of which 76% included products containing DEET and 24% of products that did not contain DEET. After inclusion of picaridin to Poisindex<sup>®</sup> in 2006, there were a total of 276 picaridin exposures (max: 42 in 2007; min: 3 in 2006). Patients were predominantly under 5 years of age (77.2%) and reported primarily as unintentional exposures (97.3%). Overall, the majority of patients were not followed for outcome as they were expected to have no clinical effects ( $n=10,954$ ; 16.1%) or only minimal clinical effects ( $n=31,086$ ; 45.8%). Of all patients followed for outcome, the majority of experienced no effect ( $n=16,727$ ; 24.6%) or minor effect ( $n=6343$ ; 9.3). In the picaridin group, the majority experienced no effect ( $n=63$ ; 22.8%) or minor effect ( $n=14$ ; 5.1%). After picaridin ingestion, only one patient experienced a moderate effect and no patients experienced major effects or death. One death was reported with ingestion of a DEET-containing product. Clinical effects were fairly consistent across each category, and most frequent effects reported included oral irritation (4%) and vomiting (3%). **Conclusion:** The majority of patients reported to ingest picaridin-containing insect repellents had no or only minor effects. This is consistent with the majority of outcomes generally reported with DEET or non-DEET containing insect repellents. Although these data are limited, unintentional ingestion of picaridin-containing insect repellent is unlikely to cause more than minor toxicity and can generally be managed outside of a healthcare facility.

## 16. Single dose activated charcoal (AC): application by medical non-professionals – a prospective single centre study on availability and quality of administration

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**Objective:** After toxin ingestion, oral AC reduces toxin absorption but delayed administration markedly decreases efficiency. Timely discussion with a Poisons Information Centre (PIC) may favour on-site application by laypersons. A PIC can further allocate cases either necessitating medical professional care (MedProfC) or cases where AC administration and observation by laypersons appear sufficient (LayC). Additional time can be saved by storing AC prophylactically at sites at risk of toxin ingestions and suitable for AC storage (SiteAptAC). However, AC application by LayC may be inferior to MedProfC regarding AC dose, time to application and incidence of side effects. **Methods:** A prospective single centre study between February 2013 and July 2014 by PIC Munich, serving a population of approximately 10,000,000. The PIC advised AC administration according to EAPCCT guidelines. LayC was recommended whenever toxin and circumstances allowed. After informed consent, study-relevant items were collected using a standardized telephone interview within 1–2 days. Ingestion sites were classified as SiteAptAC and not SiteAptAC. Questions addressed were timesaving by LayC and storage of AC; availability (proportion of SiteAptAC with stored AC); quality (influence of the following factors: LayC/MedProfC); patients' age, recommended AC dose, type of preparation (tablets/powder) on the quality of

AC administration, defined as: AC dose administered compared to the recommended dose, time needed for administration, incidence of AC-related side effects. A multiple linear regression model or appropriate statistical inter-group testing was used for analysis. **Results:** AC was recommended in 548 cases. For questions on timesaving and availability 213 cases were eligible, 137 received AC, 113 at site. In 30/113, AC was stored prophylactically. Here, median time between the call and AC administration was 5 minutes and at least 14 minutes earlier compared with all other modalities of AC acquisition/application. For quality 176 cases were eligible, 140 LayC, 36 MedProfC. The median applied AC dose was 0.38 g/kg (66.7% of recommended AC-dose). Significantly more AC was given with AC powder than with tablets. The administered AC dose was significantly inversely correlated with the recommended dose. The person giving the AC or the patient's age had no significant influence (Lay/MedProf). The only side effect reported was nausea ( $n=5$ , all laypersons). **Conclusion:** Storage of AC for prophylactic use at sites with risk of toxin ingestions saves time to administration. AC can be given safely by laypersons without relevant negative influence on AC dose, duration or severe side effects. AC powder appears superior to tablets. Storage for prophylactic use as powder should be encouraged.

## 17. Acute side effects after consumption of the novel synthetic cannabinoids AB-CHMINACA and MDMB-CHMICA

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**Objective:** In 2014, the European Monitoring Center for Drugs and Drug Addiction (EMCDDA) reported about 30 novel synthetic cannabinoids (SC), including indole and indazole-based valine derivatives carrying a cyclohexylmethyl side chain such as AB-CHMINACA and MDMB-CHMICA (also misleadingly sold as MMB-CHMINACA), which represent a new class of SC. They are full agonists with a significantly higher affinity and activity at the cannabinoid receptor type 1 (CB<sub>1</sub>) compared to JWH-018. **Methods:** Prospective observational studies of patients treated in emergency departments (ED) after recreational use of SC, in cooperation with the Poison Centre (PC) and the Institute of Forensic Medicine Freiburg. Serum and urine samples were analysed using liquid chromatography-electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS) for SC and their metabolites. Only those cases with analytically confirmed intake of AB-CHMINACA or MDMB-CHMICA and follow up were included. One case was excluded because of a high serum concentration of 3-methylmethcathinone (3-MMC). Severity was evaluated according to the Poisoning Severity Score (PSS). **Results:** In total 45 patients (40 male, 5 female, 12–48 years) were included. AB-CHMINACA was identified in 21 serum and 21 urine samples, and MDMB-CHMICA in 18 serum and 24 urine samples. In 21 cases more than one SC was present. Amphetamine

derivatives were detected in 6 cases. AB-CHMINACA was detected for the first time in July and MDMB-CHMICA in October 2014. Severity of poisoning was minor ( $n=8$ ), moderate ( $n=30$ ) or severe ( $n=7$ ). Most frequent clinical symptoms were somnolence ( $n=25$ ), tachycardia ( $n=23$ ), disorientation ( $n=19$ ), hallucinations ( $n=16$ ), vomiting ( $n=16$ ), generalized seizures ( $n=13$ ), aggressive behaviour ( $n=11$ ) and hypokalaemia ( $n=11$ ). Less frequent symptoms were psychosis ( $n=6$ ), syncope ( $n=6$ ), muscle weakness/loss of control, and amnesia (5 each). Impairment of short-term memory lasted for several weeks in one patient. Psychosis was associated with self-mutilating behaviour ( $n=1$ ) resulting in pneumomediastinum. Rigor ( $n=2$ ), moderate rhabdomyolysis ( $n=2$ ), minor elevation of creatinine ( $n=3$ ), acute renal failure ( $n=1$ ) with increased creatinine (10.8 mg/dL), hypothermia ( $n=2$ ), dysarthria ( $n=2$ ), and intermittent apnoea ( $n=1$ ) occurred less often. Electrocardiogram (ECG) changes ( $n=4$ ) and severe sinus bradycardia ( $n=1$ ) were also reported. All patients survived. **Conclusion:** The consumption of AB-CHMINACA and MDMB-CHMICA has increased since July 2014. This is alarming because of the unexpected high frequency of neuropsychiatric symptoms such as generalized seizures (29%), aggressive behaviour (25%), psychosis (13%) and syncope (13%), and the relatively large number of life-threatening courses (7 out of 45, 16%). The new SCs seem to have a higher potential for toxicity compared to first generation SCs, such as JWH-018.

## 18. Intoxications involving 3-fluorophenmetrazine (3-FPM): Results from the STRIDA project

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**Objective:** Many novel psychoactive substances (NPS) are derivatives of classic drugs of abuse. Phenmetrazine was formerly prescribed for weight management in Sweden, but was withdrawn because of the risk of abuse. 3-Fluorophenmetrazine (3-FPM) is a fluorinated analogue of phenmetrazine sold as a central stimulant through the NPS market. This report presents a case series of analytically confirmed intoxications involving 3-FPM identified within the Swedish STRIDA project. **Methods:** In STRIDA, blood and urine samples from intoxicated patients presenting in emergency departments and intensive care units throughout the country are analysed for new and traditional psychoactive substances by multi-component liquid chromatography-mass spectrometry. The method currently covers approximately 225 parent substances or metabolites and is continuously updated, as new substances are introduced on the NPS market and reference material becomes available. Data on the associated clinical features are collected from initial phone consultations with the Swedish Poisons Information Centre (PIC) and medical records. Cases were graded according to the Poisoning Severity Score (PSS). **Results:** Between November 2014 and September 2015, 3-FPM was analytically confirmed in serum and/or urine samples from 21 cases in the project. The mean age of patients was 32.6 (range 22–54) years and 81% were men. Common clinical signs reported were tachycardia (28%), agitation (22%), hallucinations (22%), seizures (17%) and dilated pupils (17%). Treatment included sedation with benzodiazepines and/or propofol. All except one case also tested positive for other NPS (e.g. isopropylphenidate, diphenidine, hexedrone, and designer benzodiazepines) and/or traditional drugs



(e.g. amphetamine, cannabis, and ethanol). The 3-FPM cases were graded as either moderate (PSS 2, 67%) or mild (PSS 1, 33%) poisonings, but none as severe or lethal (PSS 3 or 4). At the PIC, 3-FPM was first recorded in January 2015, and there were four consultations on 3-FPM and another three on "phenmetrazine" during the study period. **Conclusion:** These results emphasize the importance of bioanalytical investigation in cases of NPS intoxication. If based on statistics from consultations with the PIC, the occurrence of intoxications involving 3-FPM would have been much underestimated. The clinical signs reported in this case series resembled those of other stimulants, and the high incidence of co-exposure with other psychoactive substances makes it difficult to relate 3-FPM to a unique clinical picture. In August 2015, 3-FPM was put under legal control as a narcotic substance in Sweden. However, on the NPS market, it has already been replaced by another structural analogue of phenmetrazine, 4-FPM.

## 19. An analytically-confirmed case of benzylglycinamide consumption

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**Objective:** We present a case of analytically-confirmed consumption of benzylglycinamide, a phenyl derivative of glycine and an analogue of milacemide,<sup>[1,2]</sup> in a patient with suspected novel psychoactive substance (NPS) intoxication. **Case report:** A 21-year-old female with a history of addiction was admitted to the psychiatric ward with suspected NPS intoxication. She showed reduced emotional expression, dysphoria, and restlessness and denied any consumption of drugs of abuse. Her mother mentioned some episodes of "absence" during the previous month. Standard toxicological screening in urine, neurological examinations, standard and sleep-deprived electroencephalogram (EEG) and magnetic resonance neurography (MRN) were negative. A urine sample and a powder found by the patient's mother were sent to our laboratory for NPS screening. The analysis of the powder with gas chromatography-mass spectrometry (GC-MS), full scan mode and proton nuclear magnetic resonance (<sup>1</sup>H-NMR) proved it was N-benzylglycinamide. The benzylglycinamide transitions (precursor ion 165.05; quantifier transition 90.95, qualifier 120) used for the analysis in liquid chromatography-tandem mass spectrometry (LC-MS/MS), multiple reaction monitoring mode, were obtained through the tuning of the powder, being a certified standard of benzylglycinamide difficult to purchase from our supplier companies. Urine 1 ml with dosulepin added as internal standard, was extracted with a mixture of hexane:ethylacetate (3:1) at pH 14 and analysed by LC-MS/MS was positive for benzylglycinamide (230 ng/mL). Urine was also submitted for NPS screening [3] that involved: a generic analysis for basic, non-volatile substances by GC-MS; a screening by LC-MS/MS for NPS belonging to the classes of cathinones, benzofurans, 2C-family drugs, other amphetamine-like substances, dissociative anaesthetic and two immunoassays for synthetic cannabinoids in urine. None were detected. Samples were negative for buprenorphine, LSD,

and ecstasy. **Conclusion:** Benzylglycinamide was never commercialized and no data about its pharmacokinetic and pharmacodynamic properties in humans are available. The evidence presented here warns that N-benzylglycinamide is a possible NPS whose effects are almost completely unknown.

## References

- [1] Sussan S, Dagan A, Blotnik S, et al. The structural requirements for the design of antiepileptic-glycine derivatives. *Epilepsy Res.* 1999;34:207–220.
- [2] O'Brien EM, Dostert P, Pevarello P, et al. Interactions of some analogues of the anticonvulsant milacemide with monoamine oxidase. *Biochem Pharmacol.* 1994;48:905–914.
- [3] Papa P, Rocchi L, Rolandi L, Valli A, et al. [Research and identification of new psychoactive substances in cases of suspected intoxication in Italy.] [Article in Italian] *Italian Journal of Addiction.* 2014;4:50–56.

## 20. Ocular ischemic syndrome associated with repeated intravenous injection of cocaine and methamphetamine

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**Objective:** Methamphetamine and cocaine are commonly used drugs of abuse. We report the first case of chronic ocular ischemic syndrome secondary to intravenous (IV) injection of cocaine and methamphetamine. **Case report:** A 26-year-old female with a past medical history of IV drug abuse presented to the emergency department complaining of anxiety, palpitations, blurred and "tunnel" vision. The visual changes had been ongoing for 3 months. She admitted to a history of IV cocaine and methamphetamine use. She reported injecting herself intravenously 30 minutes prior to arrival with cocaine into a right neck blood vessel and methamphetamine into a left neck blood vessel. The patient indicated she has been doing this repeatedly for 4 months and had unintentionally punctured her carotid artery on several occasions. She reported daily tobacco cigarette use, occasional marijuana use, and denied use of other illicit drugs besides methamphetamine and cocaine. Presenting vital signs included a blood pressure of 126/85 mmHg, heart rate of 111 beats/min, respiratory rate 18, oral temperature of 36.2 °C, and pulse oximetry of 97% on room air. Pertinent physical findings included a visual acuity of 20/30 (OD) and 20/30 (OS). Confrontational visual field testing revealed diminished peripheral vision in both eyes. Ophthalmologic examination demonstrated no pupillary defect in either eye, the retinal arteries were markedly narrowed and beaded in appearance, and retinal veins were mildly dilated. Optic neuropathy was noted in both eyes with marked pallor of the optic discs bilaterally. In addition, pinpoint non-tender punctures were noted at the injection sites and ultrasound of the bilateral neck vessels and soft tissue were normal. The urine drug immunoassay was positive for amphetamines, 3,4-methylenedioxymethamphetamine (MDMA), benzodiazepines, buprenorphine, marijuana, cocaine, and opiates. **Conclusion:** Ocular ischemic syndrome is an uncommon and vision-threatening diagnosis typically associated with chronic arterial hypoperfusion to the eye.<sup>[1]</sup> We present a case of ocular ischemic syndrome we believe to be associated with the IV injection of methamphetamine and cocaine into blood vessels in the neck. It is not possible to definitively

state whether the symptoms in this patient were secondary to intracarotid administration with thromboembolic phenomenon or to systemic vasoconstrictive properties of the administered drugs. Clinicians should be alert to the practice of illicit drugs injected into neck vessels and for the potential for vascular occlusive phenomenon to impair vision and damage the optic nerve.

## Reference

- [1] Biousse V, Newman NJ. Ischemic optic neuropathies. *N Engl J Med.* 2015;372:2428–2436.

## 21. Identification of novel psychoactive substances in biological samples from patients with severe clinical toxicity in the UK: preliminary results from the Identification Of Novel psychoActive substances (IONA) study

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**Objective:** Recreational use of novel psychoactive substances (NPS) presents a challenge for health services because of the large numbers of substances emerging and a lack of information about their pharmacology and toxicology. The UK Identification Of Novel psychoActive substances (IONA) study aims to identify the NPS involved in episodes of severe acute toxicity presenting to hospital and to link detected substances with the clinical features of severe toxicity experienced by users. Here we describe the methodology of the IONA study and results from the first 21 participants recruited from two hospitals in Newcastle and London. **Methods:** Following appropriate ethical and research governance approvals, adults ( $\geq 16$  years) with severe acute toxicity (according to specific definitions) presenting to participating hospitals after suspected recreational drug exposure can be recruited with informed consent; for those individuals without capacity at the time of presentation, the support/consent of an appropriate relative/representative can be obtained. Individual consent is then sought when the patient has regained capacity. Blood, urine and/or oral fluid samples are collected and clinical features recorded using a structured data collection sheet. Samples are transferred for analysis in Newcastle together with the associated clinical data in linked anonymised format with the code held by the local clinical team. Samples are analysed by liquid chromatography-tandem mass spectrometry. **Results:** Samples were analysed from 21 patients (16 male, 5 female; median age 28, range 16–58 years) presenting between March and October 2015. The clinical and laboratory features most commonly recorded were reduced level of consciousness (14, 67%), confusion (14, 67%), agitation (10, 48%), tachycardia  $>140$  bpm (13, 62%), acidosis (9, 43%), elevated creatine kinase (8, 38%), hallucinations (7, 33%), hypertension (6, 29%) and seizures (5, 24%); 8 patients (38%) required intubation and ventilation.

Sample analysis identified NPS in 17 (81%) patients, with multiple NPS detected in 7 (33%). Detected NPS included synthetic cannabinoid receptor agonists (SCRAs) ( $n = 11$ ), 25I-NBOMe ( $n = 6$ ), methiopropamine ( $n = 3$ ), ethylphenidate ( $n = 2$ ) and mephedrone ( $n = 1$ ). Other recreational substances identified included morphine, methamphetamine, amphetamine and methadone. **Conclusion:** The feasibility of consenting NPS users and collecting and analysing samples has been established. These preliminary data demonstrate the NPS currently involved in episodes of severe toxicity in London and Newcastle. Five further hospitals are now participating in the study with others in set up, increasing the geographic spread of the study and the rate of participant recruitment.

## 22. Profile variations of drugs of abuse cases attending Emergency Department (ED) in a ten year period: The rise of cannabis

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**Objective:** The main agents involved in drug abuse cases seen in the emergency department (ED) have been steadily changing in the last decades. As a result there are radical changes in the clinical and prognosis profile. We aim to describe these variations in our ED stressing the rise of cannabis cases which have reached second place in frequency following ethanol, as a consequence of its generalized abuse among young population in Spain. **Methods:** A descriptive retrospective study of cannabis-associated cases seen in the ED from 2003 to 2012. Cases were extracted from a prospective database held by the Unit of Clinical Toxicology containing all ED acute poisonings treated in this period. It allowed us to verify the change of etiological profile and the characteristics of cannabis-related cases. **Results:** Cases involving drugs of abuse attending the ED make up approximately 50% of the total acute poisonings, which represent an average of 600 cases a year. The outstanding main agent is ethanol as a constant pattern accounting for 80% of cases. Up to 2008 the main illegal drug was cocaine but since 2009 this place has been occupied by cannabis. The total number of cannabis-associated cases over the study period was 612. The rising trend of cannabis associated cases is as follows: it was present in 4% and 15% of the study group in 2003 and 2012, respectively. There is a significant higher prevalence of cases in males (79%). The age range remains constant with a mean of 24 years (SD 2). Additional drugs were involved in most cases (71%). The clinical symptoms of the 177 cases in which cannabis was consumed alone were as follows: anxiety (20.5%), agitation (18.2%), tachycardia (18.6%) and delirium (17.1%). A few patients developed severe complications with convulsions ( $n = 10$ ), unconsciousness ( $n = 3$ ), cerebral hemorrhage ( $n = 1$ ) and stroke ( $n = 1$ ). **Conclusion:** We have found a steady rise in the number of patients presenting to the ED with exposure to cannabis. The cases are more frequent in males and patients under 26 years of age. The symptoms were mainly psychiatric and of low severity although some severe cases were reported.

## 23. Phenethylamines – they have known, but have they loved? Mass intoxication with 2C-E in northern Germany

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**Objective:** In recent years the recreational use of novel psychoactive substances (NPS) has grown. The 2,5-dimethoxy-phenylethylamine series, commonly known as the 2C series, represents a specific class of ring substituted phenethylamines with potent hallucinogenic properties.[1] The first of many 2C compounds was synthesized in 1974 by Alexander Shulgin, author of "PIHKAL (Phenethylamines I Have Known And Loved): a chemical love story".[2] Literature reports involving 2C intoxication are limited. Nevertheless, fatalities have been reported.<sup>3</sup>We report the first mass intoxication with 2C-E, which occurred during a conference for alternative and homeopathic practitioners in northern Germany in September 2015. All 29 participants voluntarily took an unknown mind-altering substance during a seminar. **Case series:** Of the 29 patients, 21 presented to hospital following the oral exposure. There were 11 female, 8 male and 2 gender unknown patients, age range 30–70 years. All patients experienced hallucinations/agitation, mild to moderate tachycardia and somnolence (unclear if sedative related). Single episode seizure and creatine kinase (CK) elevation were observed in one third of patients. A minority displayed mild hyperthermia (23.1%, 3/13). Rapid bedside toxicology screening was negative for amphetamines in all tested patients ( $n = 10$ ). Twenty patients had a moderate Poisoning Severity Score (PSS) (95.2%) and one severe (4.8%). Sedation was achieved with benzodiazepines, other sedatives were not required. Sixteen patients (76.2%) were discharged from hospital within 24 hours and 5 (23.8%) within 48 hours. Capsules found at the scene were confirmed as 2C-E by a police laboratory. Biological samples were not available pending possible legal action. **Conclusion:** The increasing popularity of NPS poses a challenge for poisons centres. 2C-E reportedly displays both hallucinogenic and stimulating effects.[3] The observed clinical features in our patients were consistent with previous reports. Adequate sedation was achieved with benzodiazepines. All patients were discharged from hospital within 48 hours. No fatalities were observed. In the words of Alexander Shulgin, father of the 2C series, "Someday, the full character of 2C-E will be understood, but for the moment, let it rest as being a difficult and worth-while material. A very much worth-while material."

### References

- Dean BV, Stelpflug SJ, Burnett AM, et al. 2C or not 2C: phenethylamine designer drug review. *J Med Toxicol.* 2013;9:172–178.
- Shulgin A, Shulgin A. PIHKAL: a chemical love story. Berkeley, USA: Transform Press, 1991.
- Srisuma S, Bronstein AC, Hoyte CO. NBOMe and 2C substitute phenylethylamine exposures reported to the National Poison Data System. *Clin Toxicol (Phila).* 2015;53:624–628.

## 24. Cross-reactivity of selected old and novel psychoactive substances (NPS) in an amphetamine and ecstasy immunoassay

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**Objective:** The increasing use and abuse of NPS has created an analytical challenge for clinical toxicology laboratories aiming to maintain a high detection rate, as well as trying to identify causes for "false" positive test results. We evaluated the cross-reactivity of selected NPS on two immunoassays (amphetamine and ecstasy). **Methods:** The drugs tested were: para-methoxymethamphetamine (PMMA), meta-chlorophenylpiperazine (m-CPP), cathinones (methylone; mephedrone; methylenedioxypropylvalerone [MDPV]); alpha-pyrrolidinovalerophenone, ( $\alpha$ -PVP), ketamine, methoxetamine and 2-oxo-3-hydroxy-lysergic acid diethylamide (2-oxo-3-hydroxy-LSD). The DRI<sup>®</sup> Amphetamines and Ecstasy Assays were used with the applications recommended by the manufacturer on an C16000 Architect instrument (Abbott Diagnostics). The cut off values were 1000 ng/mL and 500 ng/mL, respectively. The cross-reactivity was determined for pure standard solutions of drugs prepared by diluting the pure standards in blank urine at 6–1000 ng/mL Cerilliant<sup>®</sup> (Sigma-Aldrich, Barcelona). Cross-reactivity (%) was calculated using: cut off concentration/drug concentration  $\times$  100. If cross-reactivity was observed, the results were plotted as milliabsorbance/minute versus concentrations. The concentration of drug that produces an absorbance reading equivalent to the cut off was calculated by fitting a quadratic equation. **Results:** Little cross-reactivity was observed for most drugs except PMMA with both assays and m-CPP, to a lesser extent, with the amphetamine assay (Table 1). **Conclusion:** PMMA and m-CPP demonstrated cross-reactivity towards the immunoassay evaluated. The manufacturer only cites cross-reactivity of PMMA on the DRI<sup>®</sup> Ecstasy Assay (29% versus 35% in our study). Recognizing cross-reactivity can help to determine analytical confirmation strategies for individual patients.

**Table 1.** The cross-reactivity of selected drugs on amphetamine and ecstasy immunoassays.

Drug	DRI <sup>®</sup> Amphetamines Assay		DRI <sup>®</sup> Ecstasy Assay	
	Cross-reactivity (%)	Concentration	Cross-reactivity (%)	Concentration
PMMA	127	785 ng/mL*	35	1413 ng/mL*
m-CPP	6.7	15 $\mu$ g/mL*	0.05	1000 $\mu$ g/mL*
Methylone	<1	100 $\mu$ g/mL $\S$	0.63	80 $\mu$ g/mL*
Mephedrone	<1	100 $\mu$ g/mL $\S$	<0.5	100 $\mu$ g/mL $\S$
MDPV	<1	100 $\mu$ g/mL $\S$	<0.5	100 $\mu$ g/mL $\S$
$\alpha$ -PVP	<1	100 $\mu$ g/mL $\S$	<0.5	100 $\mu$ g/mL $\S$
Ketamine	<3	30 $\mu$ g/mL $\S$	<1.7	30 $\mu$ g/mL $\S$
Methoxetamine	<3	30 $\mu$ g/mL $\S$	<1.7	30 $\mu$ g/mL $\S$
2-Oxo-3-hydroxy-LSD	<3	30 $\mu$ g/mL $\S$	<1.7	30 $\mu$ g/mL $\S$

\*Concentration of drug that produces an absorbance reading equivalent to the cut off of amphetamines/ecstasy assay.

$\S$ Maximum concentration that tested negative in relation to the calibrator value cut off.

## Reference

- [1] Beck O, Rausberg L, Al-Saffar Y, et al. Detectability of new psychoactive substances, 'legal highs', in CEDIA, EMIT, and KIMS immunochemical screening assays for drugs of abuse. *Drug Test Anal.* 2014;6:492–499.

## 25. Geographical patterns in benzodiazepines involved in acute recreational drug toxicity presentations to the European Drug Emergencies Network (Euro-DEN)

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**Objective:** Non-medical use of benzodiazepines is common; however there are limited data on the acute harms related to this misuse. We describe acute recreational drug toxicity presentations involving non-medical use of benzodiazepines over the first 12 months of the Euro-DEN project. **Methods:** Data was collected on all acute recreational drug/novel psychoactive substance (NPS) toxicity presentations to Emergency Departments (EDs) in the Euro-DEN network of 16 sentinel centres in 10 European countries (Denmark, Estonia, France, Germany, Ireland, Norway, Poland, Spain, Switzerland, the UK) for 12 months (October 2013 to September 2014). Data collected from the hospital chart was: demographics, self-reported drugs/NPS used (presentations were not included in the Euro-DEN dataset if they involved deliberate benzodiazepine self-poisoning or therapeutic use of benzodiazepines), clinical features, management and outcome. **Results:** Of the 5529 Euro-DEN presentations, 1006 (18%) (73% males, mean age 36) involved non-medical use of a benzodiazepine; in 196 (19%) a benzodiazepine was the only drug. There were 18 different benzodiazepines involved, most commonly clonazepam (315), unknown benzodiazepine (259), diazepam (219), alprazolam (140), oxazepam (59), bromazepam (33), flunitrazepam (20), nitrazepam (15), lorazepam (7) and tetrazepam (3). More than one benzodiazepine was recorded in 80 presentations. Co-ingestions were ethanol (380), heroin (326), cannabis (140), amphetamine (118), methadone (109) and cocaine (93). Benzodiazepines were reported in 2–50% of presentations to each centre; the highest proportion of cases were in Drogheda, Ireland (50%), Munich (42%), Parnu, Estonia (33%), Oslo-EMA (33%) and Paris (33%). Benzodiazepines were among the top five substances reported in eight of the 16 Euro-DEN centres. Some benzodiazepines were particularly concentrated in one centre: bromazepam (94% Paris), flunitrazepam (90% Oslo-EMA), clonazepam (89% Oslo-EMA) and oxazepam (73% Oslo-EMA). Others were more widely represented across centres: alprazolam (48% Oslo-EMA, 19% Paris, 14% Mallorca, 5% Dublin and 5% Drogheda) and diazepam

(38% Oslo-EMA, 18% Paris, 11% York, 9% Dublin, 8% London-STH and 8% London-KCH). Of the patients, 51% were medically discharged from the ED, 19% self-discharged and 7% were admitted to critical care. Benzodiazepines were involved in three deaths; two unknown benzodiazepines (one in combination with methadone and cannabis) and one involving oxazepam, baclofen and zolpidem. **Conclusion:** The Euro-DEN dataset provides a unique insight into epidemiology of the acute harms associated with the non-medical use of benzodiazepines in Europe. Some benzodiazepines (alprazolam and diazepam) were geographically widely distributed and others (clonazepam, oxazepam, bromazepam and flunitrazepam) were more concentrated in a few centres.

## 26. Pattern of acute toxicity related to the use of the novel psychoactive substance methedrone (4-methoxymethcathinone, 4-MeOMC)

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**Objective:** Methedrone is a synthetic ring-substituted cathinone, and is the beta-keto derivative of para-methoxymethamphetamine (PMMA). The only information on the acute toxicity of methedrone in humans is from Internet-based user discussion forums; there have been no published case reports of acute methedrone toxicity. We describe here the pattern of acute toxicity related to the use of methedrone in cases identified from the Euro-DEN project. **Methods:** The European Drug Emergencies Network (Euro-DEN) project involves longitudinal collection of data from 16 sentinel centres in 10 European countries on Emergency Department (ED) presentations with acute drug toxicity. The 5529 cases submitted to the Euro-DEN database between 1 October 2013 and 30 September 2014 were searched to identify acute toxicity presentations involving methedrone. Data was extracted from identified cases included: basic demographics, co-used substances, symptoms/signs, initial disposition from the ED and overall length of hospital stay. **Results:** There were 92 (87 male, 5 female) acute toxicity presentations in which the use of methedrone was identified (this was the second commonest novel psychoactive substance (NPS) after mephedrone (245 presentations)). The mean  $\pm$  SD age was  $31 \pm 7$  (range 17–55) years. In total 65 (71%) presentations involved  $\geq 1$  other recreational drugs or NPS; the top five co-used were gammahydroxybutyrate/gammabutyrolactone (GBH/GBL) (39 cases), methamphetamine (19), 3,4-methylenedioxymethamphetamine (MDMA) (10), ketamine (8) and cocaine (6). Two presentations involved the co-use of mephedrone. The two commonest symptoms were agitation/aggression (33% of cases) and anxiety (32%); other symptoms included chest pain (13%), palpitations (12%), dyspnoea (10%), hallucinations (9%), seizures (7%) and psychosis (3%). On arrival in the ED, 3% had a systolic blood pressure of  $>160$  mmHg and 30% and 1% had

a heart rate greater than 100 beats/min and 140 beats/min, respectively. All patients survived; the median length of stay was 3 h 9 min (IQR 1 h 46 m to 5 h 2 m). The majority (71, 77%) were either discharged directly (58, 63%) or self-discharged (13, 14%) from the ED; of the 21 (23%) admitted to hospital, 3 (3%) and 2 (2%) were admitted to a critical care and a psychiatric facility, respectively. **Conclusion:** This is the first reported case series of acute toxicity related to the use of methedrone. From this case series, the pattern of acute toxicity related to the use of methedrone appears to be similar to that seen with other cathinones such as mephedrone and other sympathomimetic recreational drugs such as MDMA and cocaine.

## 27. Self-reported use matched with oral fluid analysis of recreational drug use in a South London nightclub

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**Objective:** Recreational drug use prevalence is estimated from self-reported survey data, however validity may vary due to inaccuracies of self-reported use and/or variation in drug content. We combined survey data with oral fluid (OF) testing to determine the reliability of self-reported survey data in a sub-population of club-goers with a high prevalence of drug use. **Methods:** This study was conducted over 4 weekend nights in March 2015 at a South London nightclub. After informed consent, participants completed a survey of self-reported drug use and provided an OF sample (Alere Certus<sup>®</sup> device). OF was analysed using liquid-chromatography-tandem mass-spectrometry (LC-MS/MS) for classical drugs and novel psychoactive substances (NPS: mephedrone, ethylphenidate, 3,4-dichloromethylphenidate, diphenidine, methoxphenidine, etizolam, flubromazepam, mebroqualone, pyrazolam, AH-7921, methoxetamine, beta-keto 2-CB [2-amino-1-(4-bromo-2,5-dimethoxyphenyl)ethan-1-one] and 20 synthetic cannabinoid-receptor agonists [SCRAs]). **Results:** Of 101 participants, 88 (87.1%) self-reported on-night drug use and 95 (94.1%) were positive on OF analysis (Table 1). Overall, there was good agreement between self-reported use and OF analysis for all drugs reported ( $p \leq 0.05$ ), other than ketamine. However, 37 (21.6%) of the 171 reported uses of an individual drug were negative on OF analysis for that drug (survey false-positive) and 40 (4.8%) of the 839 negative survey reports were positive on OF analysis for that drug (survey false-negative). Only two NPS (ethylphenidate, diphenidine) were detected in OF, these were not self-reported. **Conclusion:** There was a high prevalence of drug use, with mephedrone being the most common drug, both self-reported and on OF analysis. Only two other NPS were identified on OF analysis but they were not self-reported; no SCRAs were self-reported or identified. Overall self-reported drug use data had good agreement with OF analysis, however in a significant minority there were false-positive/false-negative survey results. This study supports the importance of work to explore biological testing to confirm and triangulate data from self-reported drug prevalence surveys.

**Table 1.** Reported "on-night" drug use and oral fluid (OF) results.

Drug	Reported on-night use	Detection in OF		No reported on-night use	Detection in OF		<i>p</i> -value
		YES	NO		YES	NO	
Amphetamine	5	2	3	96	2	94	0.011
Cannabis	6	3	3	95	0	95	<0.001
Cocaine	18	11	7	83	1	82	<0.001
GHB	31	27	4	70	8	62	<0.001
Ketamine	3	0	3	98	0	98	–
MDMA	25	20	5	76	11	65	<0.001
Mephedrone	72	69	3	29	15	14	<0.001
Methamphetamine	8	2	6	93	3	90	0.05

$p < 0.05$  was considered significant (chi-squared/Fisher's Exact).

## 28. Outpatient treatment of acute poisoning by substances of abuse: A 1-year prospective observational study

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**Objective:** Acute poisoning by substances of abuse results in hours of observation in emergency departments and many hospital admissions. Ideally, procedures should identify patients in need of hospital admission and avoid hazardous discharges, while keeping the observation time short. The Oslo Accident and Emergency Outpatient Clinic (OAEOC) has developed a simple and systematic procedure for the assessment of these patients. We assess the safety of this procedure through charting mortality and re-presentations to the OAEOC or any Norwegian hospital within the first week after discharge. **Methods:** All patients 12 years and older treated for acute poisoning by substances of abuse at the OAEOC were included consecutively from October 2011 to September 2012. Data was gathered on pre-set registration forms and observational charts. We reviewed the electronic medical records and included any missed cases or missing information. Data on re-presentations during the first week after discharge was retrieved from the local electronic medical records and from the Norwegian Patient Register. Fatalities and cause of death were obtained from the Cause of Death Register. **Results:** There were 2343 cases of acute poisoning with substances of abuse; 1600 (68%) were in males. Median age was 37 years. The main toxic agent was ethanol (1291, 55%), followed by opioids (539, 23%), benzodiazepines (194, 8%), central stimulants (132, 6%) and gammahydroxybutyrate (GHB) (105, 4%). A computerised tomography (CT) scan was done in 144/217 (66%) patients with concomitant head injury, eight were positive. Naloxone was given in 198 (8%) cases. In 391 (17%) cases the patient was admitted to hospital. Median length of stay at the OAEOC was four hours. Two patients died during the first week after discharge, both from a new opioid poisoning. In 375 (16%) cases the patient re-presented at the OAEOC or a hospital within a week, among them 13 (3%) with a diagnosis missed at the index episode, 31 (8%) for follow up of concomitant conditions diagnosed at index, 169 (45%) with a new poisoning, and 162 (43%) for reasons not related to the index episode. Among the patients with missed diagnoses, five needed further treatment for the same poisoning episode, two were admitted with psychosis, one had hemorrhagic

gastritis, one had fractures in need of operative surgery, and four had minor injuries. **Conclusion:** The procedure in use at the OAEOC can be considered safe and could be implemented elsewhere. The high re-presentation rate during the first week calls for better follow up procedures.

### 30. Increase in unintentional pediatric exposures in a recreational marijuana state

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**Objective:** Despite US Federal Schedule I status, 27 states have decriminalized medical marijuana and 4 states have passed legislation legalizing recreational marijuana.[1] In Colorado, the recreational marijuana industry became operational in January 2014. Child resistant packaging (CRP) requirements were included in marijuana legalization. Although medical marijuana decriminalization was associated with increased unintentional pediatric exposures,[2] the additional impact of recreational marijuana legalization is unclear. **Methods:** A retrospective study of cases presenting to a children's hospital (CH) and calls to a regional poison center (PC) for children 0–9 years with a marijuana exposure from 2009 to 2014 in a state with medical and recreational marijuana legalization. Rates for the PC data were calculated by dividing the number of cases in the state and the rest of the US by the corresponding populations, obtained from the US Census, and Poisson Regression was used to evaluate trends. **Results:** At the CH 46 patients presented with median age of 2.7 (1.4, 3.7) years. Of these 18 exposures (39%) involved medical marijuana; 7 of the 16 cases (44%) in 2014 involved recreational products. Infused edible products were involved in 22 cases (48%). Most patients (28, 61%) were observed in the emergency or urgent care department with inpatient admission for 11 (24%). There were 116 marijuana exposure calls to the PC with a median age of 2.0 years (IQR 1.3, 4.0). In 34 exposures (29%) the product was inappropriately stored or left in sight of the child. The majority of children had either no (24%) or minor effects (46%); there were 13 (11%) moderate and 4 (3%) major effects. The state had a 34% average annual increase in PC calls (95% CI: 17%, 54%;  $p < 0.01$ ) while the rest of the US had a 14% average annual increase in calls (95% CI: 10%, 18%,  $p < 0.01$ ); the difference was statistically significant ( $p = 0.03$ ). When compared to 2013, the annual call rate to PC for marijuana exposures significantly increased in 2014 ( $p = 0.05$ ). **Conclusion:** There was an increase in PC calls for pediatric exposures during the first year of recreational marijuana legalization, and edible products were a significant source. Identifying successful preventive strategies for pediatric marijuana exposures requires further investigation as the effectiveness of CRP remains unclear.

#### References

- [1] [cited 2015 Nov 12] [http://medicalmarijuana.procon.org/view\\_resource.php?resourceID=000881](http://medicalmarijuana.procon.org/view_resource.php?resourceID=000881)
- [2] Wang GS, Roosevelt G, Le Lait MC, et al. Association of unintentional pediatric exposures with decriminalization of marijuana in the USA. *Ann Emerg Med.* 2014;63:684–689.

### 31. ADB-Fubinaca in the real world: a case series of 15 poisonings

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**Objective:** ADB-Fubinaca is a synthetic cannabinoid that has recently been identified in herbal blends. The aim of the present study was to describe toxicity following ADB-Fubinaca poisoning in Hungary. **Case series:** At the beginning of May 2015 during a two-day period 15 patients were admitted to our department after consuming a new recreational drug. There were 8 males and 7 females. Based on the history, all patients had taken one blue-coloured tablet never used before. Each tablet was marked with the sign of a very popular Internet social networking site. The only co-ingestant was ethanol in 2 patients (13.3%). The average age was 30.3 years, only two patients were younger than 21 (range 18–48 years). The mean time to admission was 2.1 hours. We took blood and urine samples for toxicological analysis at the time of admission. Symptoms that developed were central nervous system (CNS) depression (73.3%), confusion (60%) mild tachycardia (53.3%), hypertension (33.3%), mild acidosis (26.7%), hallucinations (26.7%), anxiety (20%), agitation (20%), aggression (20%), mydriasis (13.3%) vomiting (6.7%), hypotension (6.7%) and blurred vision (6.7%). There were no cases of bradycardia, seizure, elevated temperature or extrapyramidal symptoms. There were no fatalities; one patient was intubated and ventilated mechanically because of deep coma and respiratory insufficiency. Using the Poison Severity Score, 20% of patients had mild, 73.3% moderate and 6.7% severe intoxication. All patients required hospitalization; the length of stay averaged 45.78 hours (range 11–187 hours). Therapy included IV fluids, low molecular weight heparins for thrombosis prophylaxis and pantoprazole for stress ulcer prophylaxis. Naloxone proved to be ineffective in improving the level of consciousness in the first 4 patients, so was not used in the other cases. Administration of IV benzodiazepine (midazolam) was required in 6 patients because of confusion, agitation, aggressive behaviour or hallucinations. All but 3 patients were given oxygen intranasally. As a consequence of transient agitation, 3 patients developed moderate rhabdomyolysis. The patient that required mechanical ventilation developed pneumonia. There was no other complication. One patient was moved to psychiatry because of prolonged hallucinations and psychosis. Toxicological analysis performed within 2 days revealed ADB-Fubinaca in all samples. We reported the cases to the Hungarian National Focal Point. **Conclusion:** Toxicity following use of novel cannabinoid-typed designer drugs is unpredictable. ADB-Fubinaca can cause a short period of confusion and agitation followed by long-lasting CNS depression, hypoxaemia and fluctuating changing in level of consciousness.

### 32. Specific issues in acute cannabis poisoning in adolescents

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**Objective:** To assess the specific clinical aspects of acute cannabinoid poisoning in adolescents admitted in a pediatric poison center. **Methods:** We performed a five year retrospective study

(2010–2014) of poisoned patients with drugs of abuse in whom urinary toxicological analysis revealed tetrahydrocannabinol (THC). The following parameters were analyzed: age, sex, place of consumption, clinical picture, length of stay, treatment and evolution. **Results:** Out of the total of 214 patients with acute drug of abuse poisoning, 41 had a urine sample positive for THC and diagnosis of acute cannabis poisoning. The majority of patients were boys ( $n=28$ ), with a median age of 15.9 years. Of the 41 cases, 36 poisoning occurred in a public place: in the street ( $n=16$ ), in school ( $n=12$ ) or in a nightclub ( $n=8$ ). Regarding the clinical picture the following symptoms were noted: decreased coordination in the majority of cases ( $n=36$ ), headache ( $n=19$ ), emesis ( $n=16$ ), somnolence ( $n=11$ ), chest pain ( $n=6$ ), agitation ( $n=4$ ), tremor of the extremities ( $n=4$ ), slurred speech ( $n=4$ ), lightheadedness ( $n=3$ ), aggression ( $n=1$ ), hallucinations ( $n=1$ ) and seizures ( $n=1$ ). Of the 6 patients with chest pain in one increased cardiac enzymes and terminal phase changes on the electrocardiogram were noted. The average length of stay was 1.2 days with a minimum of one and a maximum of 3 days. All the patients received symptomatic treatment. No deaths occurred. **Conclusion:** The majority of adolescents with acute cannabis poisoning presented with mild symptoms, requiring only symptomatic treatment and a short period of hospitalization.[1] Even rare, severe manifestations such as cardiac damage can occur.[2] One of the most common places where acute cannabis exposure occurred was school and it is necessary to develop educational activity to raise awareness of the risks of cannabis abuse among students.

## References

- [1] Annual Report to the European Early Warning System. In: 2014 National Report on Drugs to the EMCDDA by Reitox National Focal Point. Romania New Developments, Trends and In-depth Information on Selected Issues; [cited 2016 Feb 24]. Available at: <http://www.emcdda.europa.eu/publications/national-reports/romania-2014>
- [2] Ulmeanu C. Drugs of Abuse poisoning. In: Acute poisoning in children and adolescents. Romania: Tridona. 2015:249–52.

## 33. Novel psychoactive substance (NPS) consumption in binge drinkers: a new and potentially dangerous health risk

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**Objective:** Binge drinking is an increasingly common dangerous practice involving mainly children or adolescents and, in some circumstances (e.g. rave party, college drinking), is possibly associated with the co-consumption of substances of abuse.[1] We analyzed all cases of suspected consumption of novel psychoactive substances (NPS) in binge drinkers referred to the Pavia

Poison Control Centre. **Methods:** Cases of binge drinking in patients <25 years with blood alcohol concentration (BAC) >0.5 g/L were retrospectively reviewed (January 2010–July 2015) and assessed for: age, history, substances of abuse declared, circumstances of exposure, clinical manifestations, outcome, BAC, NPS-identified, association with classic drugs of abuse (cocaine, opiates, cannabis, amphetamine/methamphetamine), correspondence between history and the analytically identified-NPS. Cases with incomplete data were excluded. **Results:** In total 105 patients met the inclusion criteria. The lowest age recorded was 13 years (65% <18 years); 69% of cases occurred during the weekend. Substances of abuse co-consumed were: ketamine ( $n=10$ ), 3,4-methylenedioxymethamphetamine (MDMA) ( $n=5$ ), cannabis ( $n=4$ ), amphetamine ( $n=5$ ), cocaine ( $n=3$ ), energy drink ( $n=2$ ), lysergic acid diethylamide (LSD) ( $n=2$ ), gammabutyrolactone (GBL) ( $n=1$ ) and heroin ( $n=1$ ). Co-consumption of more than one substance of abuse was registered in 38% of cases. Main clinical manifestations were agitation (55%), tachycardia (38%), coma (34%), delirium/hallucinations (31%), drowsiness (28%), mental confusion (17%) and seizures (10%); no fatal cases were registered. In 65% of patients the BAC was higher than 1.5 g/L (highest BAC 3.26 g/L). Seventy-six cases were negative for NPS, while 36% of these were positive for classic drugs. In 29 patients (28%) at least one NPS was analytically confirmed. The NPS detected in biological samples (urine/blood) were MDMA ( $n=14$ ), ketamine ( $n=7$ ), methoxetamine ( $n=6$ ), gammahydroxybutyrate (GHB)/GBL ( $n=2$ ), 2C-series ( $n=2$ ), synthetic cathinones, 4-methylethcathinone (4-MEC) ( $n=1$ ), synthetic cannabinoids, JWH-073 ( $n=1$ ), atropine ( $n=1$ ) and benzofurans, APB ( $n=1$ ). Correspondence between substance declared and laboratory results was registered in 10% of cases and complete discrepancy in 45% of cases. **Conclusion:** Binge drinking is a relevant and increasing social problem related to acute and late toxic effects (e.g. brain development) especially during adolescence. Association between binge drinking and NPS may be particularly insidious. In our experience 3 out of 10 binge drinkers consumed at least one NPS. Specialist advanced laboratory support is essential to make the correct diagnosis and guide the treatment. **Acknowledgements:** Study supported by the Department for Antidrug Policies-Presidency of the Council of Ministers.

## Reference

- [1] Siqueira L, Smith VC, Committee on Substance Abuse. Binge drinking. *Pediatrics*. 2015;136:e718–e726.

## 34. Prospective cohort study to determine low risk acute ethanol intoxications risk factors

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**Objective:** The management of acute ethanol intoxication is based on evaluation and observation with the rare need for therapy or hospital facilities in the case of complications (i.e. trauma). However, these patients are often indiscriminately transferred by ambulance to busy emergency departments (EDs). Identifying low risk subjects that could be treated and observed at a lower level of care would optimize the use of resources. Our objective was to identify ethanol intoxicated patients at low risk for complications

**Table 1.** Characteristics of patients presenting with acute ethanol ingestion to a Spanish ED over a 3 month period.

	EtOH Score = 0 n = 239	EtOH Score > 0 n = 251	p Value
Male	148 (61.9%)	191 (76.1%)	0.0005 (\$)
Mean age (years)	23.4	33.5	0.0000 (*)
Spanish	70 (29.2%)	118 (47%)	0.0001 (\$)
British	120 (50.2%)	91 (36.2%)	0.001 (\$)
Arrived by standard ambulance	191 (82.6%)	182 (72.5%)	0.006 (\$)
Arrived by critical-care ambulance	1	10	–
Arrived at night (00:00–07:00)	191 (80%)	129 (51.4%)	0.0000 (\$)
Blood alcohol concentration (BAC) measured	20 (8.3%)	102 (40.6%)	0.0000 (\$)
Mean BAC (g/L)	1.99	1.78	
CT scan	1 (0.41%)	82 (32.6%)	0.0000 (\$)
Mean length of stay	4:18	6:36	0.0000 (*)
Admitted	0	15 (5.9%)	0.0001 (\$)
Returned to ED	1	7	0.039 (\$)

(\*) Wilcoxon test (\$) chi-squared test

and need for hospital-level care. **Methods:** A prospective cohort study of consecutive patients between 1 June and 31 August 2015 presenting to a Spanish ED due to ethanol. Demographic variables were collected and patients identified as ethanol (EtOH) score 0 or >0 depending on the presence or absence on a pre-determined checklist of a series of clinical items (head trauma, other trauma, agitation, seizure, prior sedation, suspected aspiration, focal neurological deficit, suspected coingestants, fever, oxygen saturations <90% or respiratory rate <10, suicidal, other somatic complaints) on arrival and at 2 hours intervals until discharge or admission. Outcomes were disposition, length of stay, need for ancillary tests and identification of clinical items during observation of EtOH score = 0 patients. **Results:** Overall 490 patients were included (Table 1), mean number of 5.3 per day (peak 14); 339 were male (69.1%). Mean age was 28.68 (SD 14.31) years; 211 were British (43%) and 188 Spanish (38%). There were no deaths. Eight patients (1.6%) returned to the ED after discharge. **Conclusion:** Patients with an EtOH Score 0 have a lower length of stay and need for hospital care. The items in the EtOH score could serve as a tool to help triage ethanol intoxicated patients to an appropriate level of care, especially in periods of high incidence (festivals, high tourism season, etc.).

### 35. Toxicity following recreational use of synthetic cannabinoid receptor agonists and the impact of legal control measures: a report from the UK's National Poisons Information Service

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**Objective:** Toxicity associated with recreational use of synthetic cannabinoid receptor agonists (SCRAs) has become increasingly common.[1] This study was performed to describe the characteristics of SCRA exposures in the UK, to compare the severity of

toxicity between commonly used branded SCRA-containing products and to examine the impact of legal control measures on the frequency and severity of SCRA-related toxicity. **Methods:** National Poisons Information Service (NPIS) telephone enquiry data were searched for SCRA-related terms (including relevant branded product names) for the 8 year period 2007–2014. Multiple enquiries about the same case were consolidated into a single record. Demographic data, reported exposure details, associated clinical features and Poisoning Severity Score (PSS) were analysed. **Results:** During the study period 510 individuals (80.7% male, median age 21 years) exposed to SCRAs were discussed with NPIS, with annual numbers increasing year on year. Commonly reported clinical features in the 433 (84.9%) patients reporting SCRA use without other substances included tachycardia ( $n = 73$ , 16.8%), reduced level of consciousness ( $n = 70$ , 16.1%), agitation or aggression ( $n = 45$ , 10.4%), vomiting ( $n = 30$ , 6.9%), dizziness ( $n = 26$ , 6%), confusion ( $n = 21$ , 4.8%), mydriasis ( $n = 20$ , 4.6%) and hallucinations ( $n = 20$ , 4.6%). The Maximum Poisoning Severity Score (MAXPSS) indicated severe toxicity in 36 patients (8.3%). Following legal control of “second generation” SCRAs (February 2013), [2] the number of enquiries continued to increase, without any change in the proportion with severe toxicity but differences were observed in the patterns of branded products involved. The three most commonly reported products were “Black Mamba” ( $n = 88$ , 20.3%), “Pandora’s Box” ( $n = 65$ , 15%) and “Clockwork Orange” ( $n = 27$ , 6.2%). A lower proportion of MAXPSS 2 or 3 enquiries were recorded for “Clockwork Orange” than for “Black Mamba” and “Pandora’s Box”. **Conclusion:** Enquiries about SCRA-related toxicity have become increasingly frequent in the UK and commonly involve young males. Legal control has not reduced the number or severity of enquiries, although changes in brands being used were observed. Differences in the severity of toxicity associated with different branded preparations may occur, although further work with larger patient numbers is needed to confirm it.

### References

- [1] Law R, Schier J, Martin C, et al. Increase in reported adverse health effects related to synthetic cannabinoid use. *Morb Mortal Wkly Rep.* 2015;64:618–619.
- [2] Advisory Council on the Misuse of Drugs. ‘Third generation’ synthetic cannabinoids (November 2014); [cited 2015 Nov 26]. Available at: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/380161/CannabinoidsReport.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/380161/CannabinoidsReport.pdf)

### 36. Trends in oral anticoagulant enquiries to the UK National Poisons Information Service: a retrospective 5-year review

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**Objective:** The vitamin K antagonists (VKAs), principally warfarin are used widely as anticoagulants for the long-term treatment of venous thromboembolism and thromboembolic prophylaxis in



atrial fibrillation. Their use is complicated by a narrow therapeutic index, extensive interactions and a requirement for routine monitoring. The novel oral anticoagulants (NOACs) provide effective anticoagulation without the need for coagulation monitoring. Concern has been expressed regarding the safety of the NOACs after overdose because of the previous lack of licensed antidotes to counter excessive anticoagulation in the haemorrhaging patient. We examine patterns of poisoning from newer oral anticoagulant medicines. **Methods:** Data concerning telephone enquiries to the National Poisons Information Service were sourced from the UK Poisons Information Database (UKPID) for a retrospective examination of enquiries received between the 2008 and 2013. The database was searched for: acenocoumarol, apixaban, dabigatran, phenindione, rivaroxaban and warfarin. Data were analysed by the chi-squared test. Fisher's exact test was used in comparisons which contained a numerical value less than five. A  $p$ -value of less than 0.05 was considered to be statistically significant. **Results:** A total of 1390 enquiries regarding oral anticoagulants were received during the time period, including 1280 (92%) related to warfarin, 13 (1%) to other VKAs and 97 (7%) to NOACs (rivaroxaban 65, dabigatran 29, apixaban 3). Enquiries concerning NOACs increased as a proportion of all oral anticoagulants from 0.5% in 2009 to 19% in 2013. Eighty-three percent were reported as asymptomatic exposures, 15% were symptomatic and in 2% the clinical features were unknown. The number of cases that were symptomatic was 193 (14%) for warfarin, 7 (24%) for dabigatran and 4 (6%) for rivaroxaban. A significantly higher proportion of dabigatran cases were symptomatic compared to rivaroxaban,  $p = 0.04$ , but not compared to warfarin,  $p = 0.3$ . **Conclusion:** The proportion of enquiries involving NOACs has increased to almost a fifth of oral anticoagulant enquiries. The majority of exposures to both warfarin and NOACs were asymptomatic. There appeared to be variation in the proportions of symptomatic cases between the most commonly encountered NOACs. Further data, including demographic and prescription data, are required to investigate this preliminary finding.

### 37. AfriTox<sup>®</sup> TeleLog: the development of a novel web-based data collection tool for poison centre call data in South Africa

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**Objective:** Poison centre call data describing poisoning exposures is an important source of information for administrative, medico-legal and research purposes, and is essential to the toxicovigilance role of poisons centres. Such call data is scarce worldwide, particularly in the developing world. In 2013, the Poisons Information Centre (PIC) at Red Cross War Memorial Children's Hospital (RCWMCH) set out to develop the AfriTox<sup>®</sup> TeleLog as a simple and reliable data collection tool for its poison call data. The system is linked to the AfriTox<sup>®</sup> poisons information database used widely throughout Southern Africa. **Methods:** The RCWMCH PIC received poisons calls from 2011, recording call data in a

book-based system. During 2013, a real-time database was developed enabling call data to be entered directly into the database by the Specialist in Poisons Information (SPI) on duty. FileMaker<sup>®</sup> software was used and there was extensive collaboration between the software designer and RCWMCH SPIs to create an appropriate and user-friendly tool from which accurate reports could be extracted. Sequential tabbed pages with drop-down menus prompt specific information to be entered including details of the subject, nature of the exposure and characteristics of the substances, as well as free text fields for clinical details (including Poisoning Severity score), advice given and follow up. **Results:** The AfriTox<sup>®</sup> TeleLog became operational in 2014 at the RCWMCH PIC with 1858 calls recorded during the first year. Retrospective data from 6155 calls received between 2011 and 2014 was transcribed into the database. During 2015, the AfriTox<sup>®</sup> TeleLog was further developed into a web-based system to support the creation of a single 24/7 national poisons helpline. This helpline is available to the public and healthcare professionals, and is staffed by members of the RCWMCH and Tygerberg Academic Hospital PICs, the two major poison centres in South Africa. Overall the AfriTox<sup>®</sup> TeleLog has functioned well, although issues of connectivity can hamper consistent real-time data capture at remote sites. It has become an excellent source of poisons data for South Africa containing details on over 12,000 calls. Since the introduction of the national helpline, call numbers have increased significantly with an average 775 calls per month. **Conclusion:** The AfriTox<sup>®</sup> TeleLog database is achieving its goal of facilitating real-time collection of good quality poison centre call data. While ongoing refinement of the AfriTox<sup>®</sup> TeleLog is necessary, as well as mentoring of SPIs using it, it is becoming a national asset to South Africa's health service.

### 38. Antidotes network: is it possible to connect stocks between centers?

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**Objective:** Antidotes are essential drugs for management of acute intoxications. The lapse of time from the contact with the toxic agent until antidote administration can determine patient survival. Pharmacy Departments are responsible for warranting an optimal qualitative and quantitative stock of these drugs. However, a national regulation about stocking of antidotes in hospitals is lacking, so availability problems can be an important concern. In this context, an "Antidotes network" has been proposed in our region (Xarxa d'antídots de Catalunya [Catalan Antidote Network]). **Methods:** A working group, including pharmacists and physicians with experience in the field of Clinical Toxicology, was established under the framework of the Catalan Society of Clinical Pharmacy to develop the network. Firstly, the group produced a document with recommendations about stocking of antidotes according to hospital complexity and location. Then an online application was designed to be used as a tool for communication between centers. The application gathers information about 15 antidotes, selected according to criteria such as difficulties in availability,

urgency, frequency of use or cost (digoxin antibody fragments, methylene blue, deferoxamine, dimercaprol, sodium calcium edetate, ethanol, physostigmine, fomepizole, glucagon, hydroxocobalamin, pyridoxine, pralidoxime, silibinin, botulinum antitoxin and snake venom antisera). This tool makes information about the stock in each center (including expiry date) available and facilitates antidote borrowing between hospitals. **Results:** The online application (accessible through [www.xarxaantidots.org](http://www.xarxaantidots.org)) was launched in July 2015. It has an open zone with information about the project and offers the option to ask non-urgent toxicological questions to the group experts, and a private zone accessible with username and password for those centers that have joined the network. So far 34 Catalan hospitals that provide emergency care have joined. In each center there is a pharmacist and a physician from the Emergency Department responsible for the network. These figures are denominated "farmatox" and "urgetox". The "farmatox" is in charge of the stock maintenance, updates the drug movements and helps with borrowing and lending antidotes between hospitals. The "urgetox" develops the functions of toxicology referent from the Emergency Department. **Conclusion:** The Antidote Network could allow improved communication between centers involved in the management of poisoned patients, help in adjusting and harmonizing antidotes stock and accelerate antidote borrowing, if required.

### 39. Extraordinary mobilizations of antidotes from the National Stockpile to hospital emergency departments: an example of versatility and integration of national functions and systems

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**Objective:** Since 2005, the Italian State has established an extraordinary endowment of antidotes for terrorist chemical and radioactive events (Scorta Nazionale Antidoti [SNA]). Charged by the Ministry of Health, the Pavia Poison Control Centre (PPCC) is the clinical unit responsible for (i) the diagnostic-therapeutic specialist consultation for non-conventional attacks, (ii) SNA operational management (e.g. upgrade, distribution, planning), and (iii) the continuous training of the Italian NHS. SNA is organized on a national scale (regional and national stockpiles, located in hospitals and in State deposits, respectively), and is an intangible stockpile whose integrity is essential to fulfil its functions. However, when an absolute shortage of an antidote occurs in NHS hospitals and the antidotal treatment of intoxicated patients is necessary, a quota of the SNA stockpile can be extraordinarily mobilized. Operational procedures need a clinical evaluation by the PPCC first, and then an on-time authorization by the Ministry of Health. Rapid replacement of the mobilized amounts by the requiring hospital is a procedural obligation. We evaluated the SNA's extraordinary mobilizations (SNA-EM) in a seven-year period. **Methods:** We investigated all SNA-EMs authorized or made in the period 2008–2014. For each mobilization (i) the cause of the extraordinary request (clinical indication, antidote availability/shortage in neighboring hospital and Poison Centers), (ii) the time required

for antidote arrival to the requiring hospital and (iii) the SNA stockpiles involved were assessed. **Results:** Exceptional mobilizations from the SNA to NHS hospitals were performed 25 times (for 28 patients), always linked to single/multiple poisoning from conventional causes/events. The mobilized antidotes were pralidoxime ( $n = 17$ ), succimer (DMSA) ( $n = 3$ ), unithiol (DMPS) ( $n = 2$ ), hydroxocobalamin ( $n = 1$ ), methylene blue ( $n = 1$ ) and Prussian blue ( $n = 1$ ). In 21 cases, SNA-EM occurred to hospitals located in the same region as the SNA deposit and in 4 cases in different regions. In some cases, the mobilized antidotes (unithiol, Prussian blue and succimer) are rarely used and difficult to find in NHS hospitals. **Conclusion:** SNA is an essential facility in order to have the necessary antidotes in case of exceptional events. The current organization of SNA, considered highly important in the EU, combines clinical toxicological expertise and antidote supply in order to obtain diagnostic and therapeutic appropriateness. This organization has proven useful and able to overcome hospital shortcomings of normal/rare antidotes in cases where toxic agents are unusual or the need for antidotes exceeds normal hospital availability. **Acknowledgements:** Support of Ministry of Health (4393/2013-CCM).

### 40. Profile and risk assessment of household cleaners as evaluated from Emergency Department (ED) cases in the Spanish Toxic Surveillance System (STSS) in the last 5 years

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**Objective:** The chemical substances marketed as household cleaning agents are a toxic hazard which is closely in contact with the general population. We aimed to evaluate the profile and risk of exposure to household cleaning agents in patients that attended the ED collaborating with the STSS. **Methods:** We analysed the cases attending the ED of 21 public hospitals due to exposure to irritant gases, caustics, solvents and detergents from 2010 to 2014. **Results:** There were 2175 cases which represent 49% of the total cases included in the STSS over the study period. Mean age was 36 years (SD 25). Sex distribution was even with 49% male (mean age 35 years) and 51% female (mean age 41 years). Domestic accidents accounted for 1415 cases (65%) with a mean age of 36 years and higher numbers of females (57%). The main substances involved were caustics (44%) followed by detergents (21%), irritant gases (21%) and solvents (12%). There were 10 severe cases and 5 deaths (0.35%). Occupational accidents accounted for 318 cases (15%) with a mean age of 39 years and higher numbers of men (64%). The main substances involved were caustics (35%), irritant gases (34%), solvents (24%) and detergents (7%) producing one severe case and no deaths. Suicidal gestures accounted for 304 cases (14%) with a mean age of 47 years with even numbers by gender. The main substances involved were caustics (75%) followed by solvents (12%) and detergents (12%) and just one case involving irritant gases. There were 34 severe cases and 24 deaths (8%). Overall there were 435 cases involving children (up to 16 years old) with a significantly higher number of males (57%). The main substances involved were caustics (38%) and detergents (34%) followed by solvents (16%) and irritant gases (7%). There are no severe or lethal cases

involving children. **Conclusion:** The global group of household cleaning products has a profile of low risk with a proportion of severe cases of 2.34% and a mortality of 1.51%. The severe and lethal cases were mainly due to suicide attempt involving caustics. It is worth stressing that one-third of the lethal cases were due to ingestion of salfuman (hydrochloric acid marketed for domestic use). No severe cases occurred in children.

## 41. Adverse drugs reactions (ADR) collected by medical-staffed ambulances: a pilot study with the SAMU de Paris

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**Objective:** In Paris, emergency medical assistance is run by the “SAMU de Paris”. Medical-staffed ambulances go directly to any patient with an acute medical problem after evaluation of the clinical situation over the telephone. The aim of the study was to determine whether the SAMU de Paris allowed collection of adverse drug reactions (ADR). **Methods:** Every month, forms from all medical interventions performed by the SAMU de Paris, were analysed retrospectively by a physician trained in pharmacovigilance. The following information is available: patient characteristics, description of the medical event, diagnosis and outcome. If an ADR is present or even suspected, a copy of the form is made. The pharmacovigilance centres follow up with medical staff to retrieve more information about the final diagnosis and drug involvement. If an ADR is confirmed, the case is anonymously registered in the national database. **Results:** From January to March 2015, 100 cases of possible ADRs were collected while only 8 cases were spontaneously declared to the Centre Regional de Pharmacovigilance (CRPV). Of the 100 cases 68 ADRs were immediately diagnosed and registered (Table 1). Causality is pending for 23 cases. The main effects observed were cardiovascular (cardiac arrest, bradycardia) ( $n=9$ ) and neurological (coma, confusion) ( $n=9$ ); other effects were malaise, skin reaction, gastrointestinal perforation, hypoglycaemia and renal failure. For the remaining 9 cases, drug causality has been definitely ruled out, with no drug intake ( $n=5$ ), and another causative agent for 4 cases (illicit substances  $n=2$ , food  $n=2$ ). **Conclusion:** To our knowledge, this is the first time that serious ADRs have been collected directly from first responders, before hospitalization. Except

**Table 1** Main characteristics of ADRs collected by the SAMU de Paris.

Event	Number (% total)	Drugs suspected (more than one can be suspected)
Intentional drug overdose	27 (40%)	Psychotropic (24), paracetamol (2), potassium (1), digoxin (1), methadone (1)
Bleeding	14 (20%)	Oral anticoagulant (8), low molecular weight heparins (4), antiplatelet (2)
Hypoglycaemia	12 (18%)	Insulin (12)
Anaphylaxis	6 (9%)	Antibiotics (4), non-steroidal anti-inflammatory (2), neuromuscular blocker (1)
Miscellaneous	9 (13%)	Psychotropic (5), antituberculosis agents (2), analgesic (2), antibiotic (1), corticosteroid (1)

intentional drug overdose for suicide attempts, the main ADRs observed are expected, such as bleeding with anticoagulants or hypoglycaemia with insulin. Further analysis on cardiovascular effects is pending the late phase of poisoning. This limitation can be corrected at least by prospective follow up studies.

## 42. Improper use of a medicine bottle to prepare an e-cigarette refill liquid

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**Objective:** Over the last few years, electronic cigarettes (e-cigarettes) have become increasingly popular. Nicotine concentrations in the refill liquid (e-liquid) vary between 0 and 26 mg/mL, potentially reaching high-risk concentrations. This is a particular danger for children, in whom the absorption of only 2 mg orally or 0.1 mg dermally can produce signs and symptoms of acute nicotine intoxication.[1] Here we report a case in which a vial of e-liquid was mistakenly taken for a bottle of a mucolytic drug solution. **Case report:** A 3-year-old child (weight 15 kg) was admitted to the Emergency Department (ED) for nicotine intoxication. The child had mistakenly been administered 10 ml of e-liquid instead of the same amount of carbocisteine. The total amount of nicotine ingested was 80 mg (concentration of nicotine in the do-it-yourself e-liquid: 8 mg/mL, 0.8%), with an unknown amount of glycerine and propylene glycol. The child's mother reported that two vomiting events occurred within a few minutes after ingestion. In the ED, the child presented with drowsiness and paleness. An electrocardiogram (ECG) did not show any alterations except for a high heart rate (130 beats/minute); blood pressure was 102/70 mmHg and the percutaneous oxygen saturation was 99% on room air. Activated charcoal was administered. The state of consciousness improved within 40 minutes, and tachycardia resolved in a few hours. **Conclusion:** Despite the significant amount of nicotine ingested (5.3 mg/kg) and the fast absorption through all routes of exposure of liquid nicotine, the symptoms were mild and the amount of nicotine absorbed may have been reduced by the two episodes of vomiting and by the administration of activated charcoal. Notwithstanding the ingestion of e-liquid containing nicotine could lead to serious poisoning especially in children. Regulations concerning packaging and product design for refill liquids are still lacking. We deem it important and necessary that users, manufacturers, and healthcare providers consider these preparations as a potential danger.

## Reference

- [1] Smolinske SC, Spoerke DG, Spiller SK, et al. Cigarette and nicotine chewing gum toxicity in children. *Hum Toxicol.* 1988; 7:27–31.

### 43. E-cigarettes and synthetic cannabinoids: a new trend

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**Objective:** Electronic cigarettes (e-cigarettes) have become increasingly popular both for using nicotine and, more recently, for drugs of abuse. We present what we believe to be the first reported case of a patient using an e-cigarette to vaporize (“vaping”) synthetic cannabinoids (K2) for intoxication. **Case report:** A 36-year-old male with a history of alcohol and drug abuse was brought to the emergency department (ED) by ambulance for altered mental status after being found “kicking” and “rolling around on the sidewalk”. At the scene, the patient was holding an e-cigarette which he explained to paramedics he had filled with K2 to get high. In the ED, the patient’s vital signs were blood pressure 151/56 mmHg, heart rate 106 beats/min, respiratory rate 20/min, oxygen saturations 94% and temperature 37.1 °C (axillary). A finger-stick blood glucose was 116 mg/dL. His physical examination was remarkable for severe agitation, which spontaneously resolved. Laboratory studies were significant for creatine kinase 3936 U/L, negative serum ethanol, and a negative urine drug immunoassay. Electrocardiogram (EKG) showed normal sinus rhythm with a rate of 100 and non-specific T wave and ST segment changes. The patient was given intravenous fluids for his rhabdomyolysis. Serial neurological examinations demonstrated no improvement over a 4 hour period. A computed tomography (CT) scan of the head was normal. The patient was admitted for further treatment of his rhabdomyolysis and serial neurological examinations. Over the next 36 hours, the patient’s mental status and creatine kinase normalized, and he left against medical advice on hospital day three. **Conclusion:** There has been a resurgence of synthetic cannabinoid use in the US beginning in April 2015. As this case illustrates, vaping synthetic cannabinoids via e-cigarettes can lead to serious toxicity. Whether this method of use leads to greater or lesser toxicity than traditional smoking has yet to be determined. Regardless, it is important for physicians to be aware of emerging trends of abuse.

### 44. Dermal and ocular exposure to vinegar essence in Austria, 2002–2014

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**Objective:** Household vinegar contains up to 25% acetic acid, but industrially used vinegar may contain up to 80% acetic acid. Unfortunately, this high percentage acetic acid can be purchased at wholesale and via the Internet. Vinegar essence is used in households as a descaling agent, cleaning agent and strongly diluted as a salad dressing. We performed a retrospective analysis of calls regarding dermal and ocular exposure of vinegar essence. **Methods:** Cases from the Poison Information Centre database involving acute dermal and ocular exposures to vinegar essence were evaluated for the period of 2002–2014. All exposures were accidental and in most cases the amount of vinegar essence involved was unclear. **Results:** Over the 13 year period, 25 cases of dermal, 2 cases of ocular and 2 of dermal and ocular exposure to vinegar essence were documented (see Table 1). Of these, 24 patients developed chemical burns of the skin or eyes. Three

**Table 1.** Accidental dermal and ocular exposure in adults and children exposed to vinegar essence.

Symptoms	>15 years			11 Months–10 years
	Dermal n = 13	Ocular n = 2	Dermal + ocular n = 2	Dermal n = 12
None	1	0	0	1
Irritation	1	0	0	2
Chemical burn	11	2	2	9

patients showed only irritation of the skin. In two cases there were no symptoms at all, so the exposure was classified as questionable. In three well documented paediatric cases (16 months, 22 months old and a child of unknown age) vinegar essence was applied topically in order to lower fever. All these children showed clinical signs of infection due to their illness and chemical skin burns on both legs, but no systemic complications occurred. Ocular exposure resulted in conjunctivitis without permanent damage. **Conclusion:** Topical exposure to organic acids has been reported to cause chemical skin burns resulting in systemic effects,[1] and is a particular risk after prolonged contact involving a large area of skin. Topical applications of acetic acid have been reported to result in chemical burns, but systemic effects have not been described so far. In our small series of well documented cases, dermal exposure to vinegar essence caused chemical skin burns without systemic toxicity. Awareness regarding the risks of systemic effects after chemical burns is indicated, however the risk is low.

#### Reference

- [1] Korkmaz A, Sahiner U, Yurdakök M. Chemical burn caused by topical vinegar application in a newborn infant. *Pediatr Dermatol.* 2000;17:34–36.

### 45. Household cleaning product exposures: data from the Moroccan Poison Control Centre (2010–2014)

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**Objective:** Household cleaning products are heterogeneous. These are chemical compounds for multiple uses (cleaning clothes, floor, drains, dishwasher products, bleach, etc). The pipe drain cleaners, concentrated bleach and dishwasher salt, are responsible for very serious accidents.[1] We sought to describe the epidemiological profile of household cleaning product exposures, and particularly the circumstances of intoxication in cases reported to poison control centre of Morocco. **Methods:** A retrospective study of cases of household cleaning product exposure reported to the Centre anti-poison du Maroc (CAPM) over a 5 year period (2010 to 2014). All the cases were analyzed for demographic features, circumstances, clinical consequences, products and evolution. **Results:** Information on 2353 cases was collected; these cases accounted for 4.7% of all poisoning cases over this period. The average age of our patients was 17 ± 9.45 years (range 1 to 98 years). Sex ratio was 0.7. Adults and children (<5 years of age) were most commonly involved, 65.8% and 9%, respectively. Accidental poisoning was most common in children (62%). Suicide attempts occurred in 38% of cases. The home was the most common location where the poisoning occurred (94%).

The most incriminating household cleaning products were bleach (69.3%) followed by spirit of salts (hydrochloric acid) (11.6%). The most frequent exposure routes were ingestion (93.6%) following by inhalation (55.1%) and eye contact (1.3%). Patients were symptomatic in 71.1% of cases. The most commonly reported symptoms were gastroesophageal (96%). The outcome was favourable in 94.9% of the cases. Sequelae occurred in 4.6% of cases and death in 0.5% (64.2% of deaths were in adults). **Conclusion:** The poison control centre of Morocco has implemented a strategy to reduce deaths by cleaning products. This has involved various strategies including a specific review of cleaning product exposure, legal restriction of the sale of hazardous household products, safety packaging and prevention awareness campaigns.

## Reference

- [1] Rauber-Lüthy C, Kupferschmidt H. Household chemicals: management of intoxication and antidotes. *EXS*. 2010;100:339–363.

## 46. A fatal human exposure to sodium dichloroisocyanurate tablets

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**Objective:** Sodium dichloroisocyanurate in contact with stomach acid produces an exothermic reaction which can liberate chlorine gas, which can result in respiratory distress if liberated chlorine is inhaled.[1] Toxic pulmonary oedema and cardiovascular failure can occur if the poisoning takes a fulminating course.[1] We describe a fatal ingestion of household sterilising tablets containing sodium dichloroisocyanurate. **Case report:** A 73-year-old male patient presented to the Emergency Department following a suspected ingestion of two Diversity Titan Chlor tablets<sup>®</sup> containing 20–30% sodium dichloroisocyanurate and 3–10% sodium carbonate. They were thought to have been chewed as he was found with white residue in and around his mouth. He was discharged after a brief period of observation but he re-presented 24 hours after ingestion with dysphagia and clinical symptoms of bilateral pneumonia, which was later confirmed on a chest X-ray. Investigations taken on re-presentation revealed metabolic acidosis (lactate 5.3 mmol/L, bicarbonate 18 mmol/L), blood glucose 19.6 mmol/L, haemoglobin 138 g/L, white cell count  $12.8 \times 10^9/L$ , platelets  $143 \times 10^9/L$ , prothrombin time 12 s, activated partial thromboplastin time 26 s, fibrinogen 5.4 g/L, albumin 47 g/L, alkaline phosphatase 73 U/L, alanine transaminase 17 U/L, bilirubin 29  $\mu\text{mol/L}$ , sodium 144 mmol/L, potassium 4.4 mmol/L, urea 9.0 mmol/L, chloride 77 mmol/L and C-reactive protein 194 mg/L. In view of frailty and dementia and his deteriorating condition he was deemed unfit for aggressive intervention and was transferred to the intensive care unit and treated with intravenous piperacillin/tazobactam, fluids and oxygen. Despite supportive treatment, his condition deteriorated, treatment was withdrawn and he died six days post-ingestion. The post-mortem examination report did not mention corrosive injuries. **Conclusion:** There are only a few similar cases reported. The characteristic symptoms upon presentation to the emergency department include vomiting and stridor.[2] All previously reported cases involved ingestion of one tablet and were treated successfully without sequelae. In this case, the patient ingested two tablets, had delayed onset of features, pre-existing co-morbidities and a delay in treatment. These may have been contributing factors to the fatal outcome of this patient. Ingestion of two tablets containing 20–30% sodium dichloroisocyanurate may be fatal.

## References

- [1] Okonek S, Reinecke HJ, Krienke EG, et al. [Poisoning by hypochlorite-containing disinfectants. A retrospective analysis of 594 cases of poisoning.] [Article in German] *Dtsch Med Wochenschr*. 1984; 109:1874–1877.
- [2] Siodlak MZ, Gleeson MJ, Wengraf CL. Accidental ingestion of sterilising tablets by children. *Br Med J (Clin Res Ed)*. 1985;290:1707–8.

## 47. Accidental poisonings by ingestion of decanted liquid chemicals: Retrospective analysis of cases reported to a Poisons Centre 1997–2011

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**Objective:** Poisonings by ingestion of decanted chemicals are regularly observed by Poisons Centres, however data describing such incidents are limited.[1,2] **Methods:** A retrospective review of cases with accidental ingestion of liquid chemicals, stored in another container than the original one, which were reported to a Poisons Centre from 1997 to 2011, was conducted. The clinical course was compared to all cases with accidental ingestion of chemicals. **Results:** In total 1121 exposures to decanted chemicals were reported, corresponding to 0.34% of all calls regarding exposures during the same period. In 818 cases adults ( $\geq 16$  years) were affected and 303 involved children ( $< 16$  years). In 754 cases the chemical was stored in a soft-drink bottle, in 361 in another bottle, in 6 in another container. In 669 (59.7%) cases a household product was involved, in 338 (30.1%) an industrial, in 95 (8.5%) an agricultural and in 19 (1.7%) an unknown product. In 538 of the cases treatment by a physician was documented, including 431 in hospital. The most frequently reported effects at initial call were mild gastrointestinal, neurological and respiratory symptoms. Final outcome was known in 382 cases where a follow up by a physician was available. It was classified as no effect in 56, mild in 282, moderate in 37 and severe in 7 cases; no deaths occurred. Severe effects were caustic injuries of the gastrointestinal tract, epiglottic oedema, coma, aspiration pneumonia and acidosis. In 27 (61.4%) of the moderate and severe cases industrial products, often containing corrosives or hydrocarbons, were involved. In the same period 5432 cases with follow up and oral exposure to a chemical stored in the original container were reported. A symptomatic course was significantly more frequent with decanted chemicals (85.3% and 59.1%, respectively; odds ratio 4.02; 95% CI 3.01–5.37;  $p < 0.0001$ ). Ingestion of an industrial product was more frequent in cases with decanted products (38.5% and 25.4%, respectively). **Conclusion:** Poisonings with decanted chemicals are rare in Switzerland, but they cause clinical signs in a high percentage of cases, often requiring treatment. Moderate and severe symptoms were more frequent in cases with ingestion of industrial products, especially products containing hydrocarbons or corrosives.

## References

- [1] Cassidy N, Tracey JA. Morbidity and mortality following inadvertent poisoning with decanted chemicals. *Ir Med J*. 2005;98:175–178.
- [2] Geller RJ, Kezirian R, Bangar P, et al. Epidemiology of accidental poisoning caused by storage of non-food substances in food containers and unmarked bottles/containers. *Clin Toxicol (Phila)*. 2009; 47:705.

## 48. Laundry detergents capsules: experience of the Spanish Poisons Center

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**Objective:** Use of laundry detergent capsules (CDR, its Spanish acronym) is widespread. Anionic and non-ionic surfactants are the main ingredients in standard laundry detergents.[1] Since toxicity is directly correlated to surfactant concentration, capsules (50% anionic surfactant) are more dangerous than powder (20%). In the capsules the concentration range is 2.5–5% higher. CDRs appeal to children because of their vivid colour, and they can play with them and may bite them. The main clinical effects are gastrointestinal symptoms and respiratory problems. The objective is to report CDR exposure cases recorded by the Toxicology Information Service (SIT). **Methods:** A retrospective study of reported exposures to CDRs between 1 January 2008 and 30 June 2015 recorded in the SIT database. SIT manages a database with over 179,000 files of potentially poisonous products marketed in Spain with its corresponding toxicological profile, which enables accurate and quick medical response in poisoning cases. Notification of product composition to SIT is mandatory in agreement with current regulations.[2,3] **Results:** In total 994 cases involving CDRs were recorded. The representative profile corresponds to a male aged 19–24 months, ingesting part of a capsule. Adverse health effects were gastrointestinal, respiratory and cutaneous. **Conclusion:** It is critical to strictly follow hazard advices for cleaning products, particularly with CDRs, considering the higher risk in the youngest members of the population. Preventive measures against exposure in children (especially below 6 years) should focus on safe packaging and clearly displayed warnings on the label of all potential risks. SIT collaborates with ADELMA (Spanish Association of related cleaning products) and the European detergent industry in its campaign to promote safe use of these products. As a result of several reports provided by poison centers, manufacturers are implementing specific safety actions for chemicals marketed in Europe.

## References

- [1] Martínez R, Mencías E. Productos de limpieza domésticos. In: Mencías Rodríguez E, Mayero Franco LM, eds. *Manual de Toxicología básica*. Madrid, Spain: Ed. Díaz de Santos; 2000:452–4.
- [2] Real Decreto 770/1999, de 7 de mayo, por el que se aprueba la Reglamentación técnico-sanitaria para la elaboración, circulación y comercio de detergentes y limpiadores. *Boletín Oficial del Estado*, 18 de mayo de 1999, núm. 118, de 18 de mayo de 1999, 18545–51.
- [3] Commission Regulation (EU) No 453/2010 of 20 May 2010 amending Regulation (EC) No 1907/2006 of the European Parliament and

of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). *OJEU* 2010;L133/1–43.

## 49. Exposure to liquid laundry detergent capsules: experience of the Danish Poisons Information Centre

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**Objective:** In 2012 liquid laundry detergent capsules (LLDCs) were introduced in Denmark as a more convenient method to package soap intended for washing machines. LLDCs can be mistaken for toys, and severe poisonings in toddlers have been reported in several case studies.[1,2] The objective of this study was to evaluate the estimated health risk caused by exposure to these products based on exposure data from the Danish Poisons Information Centre (DPIC). **Methods:** A retrospective study based on the systematic registration of enquiries to the DPIC regarding exposure to LLDCs. The observation period was August 2012 to October 2015. All registrations on the cases, including poisoning severity grading, were performed systematically and immediately following the call. **Results:** In total 168 cases were registered (121 calls from citizens, 47 calls from healthcare services); 4 cases in 2012, 49 cases in 2013; 59 cases in 2014 and 56 cases in 2015. The median age of the patients was 2 years (range 8 months to 67 years). Most exposures took place at home ( $n=160$ ) by accident during play ( $n=121$ ). The route of exposure was mainly oral ( $n=136$ ), followed by eye ( $n=25$ ) and skin ( $n=4$ ). Most frequently reported symptoms were vomiting ( $n=52$ ) and redness and irritation of the eyes ( $n=21$ ). In 82 cases no symptoms were reported. Risk assessment overall was no or mild risk ( $n=125$ ); moderate ( $n=35$ ) and severe risk ( $n=1$ ). About 30% of exposed patients were recommended further examination at a healthcare facility. **Conclusion:** The reported effects observed after exposure to LLDCs were very similar to those resulting from exposure to other detergents in the DPIC. Only one case was assessed as a severe poisoning. The number of registered exposures per year increased in the observation period. A greater awareness from manufacturers and consumers of the dangers and risks of the liquid laundry detergent capsules would be desirable.

## References

- [1] Lauren G. Pick your poison: what's new in poison control for the preschooler. *J Pediatr Nurs*. 2015;30:395–401.
- [2] Beuhler M, Gala P, Wolfe H, et al. Laundry detergent "pod" ingestions: a case series and discussion of recent literature. *Pediatr Emerg Care*. 2013;29:743–747.

## 50. Composition of automotive screenwashes sold in the UK: how many contain $\geq 3\%$ w/w methanol?

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**Table 1.** Concentration of methanol and presence of ethanol in screenwash products sold in the UK.

Methanol concentration %	All products ( <i>n</i> = 163)	Co-formulated with ethanol ( <i>n</i> = 115) (%)
<3%	58	54 (93%)
≥3%	39	15 (38%)
May contain ≥3%†	66	46 (70%)
[Possible total ≥3%	105	61(58%)]

†Includes 56 products containing 1–5% (37 co-formulated with ethanol); 9 products containing 1–10% (8 co-formulated with ethanol); 1 product containing 1–3% (co-formulated with ethanol).

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**Objective:** In 2015, the European Chemicals Agency and its Committee for Socio-Economic Analysis considered a request from two European Union countries to restrict the placing on the market (for supply to the general public) of screenwashes that contained methanol at concentrations at or above 3% w/w. The UK National Poisons Information Service (NPIS) was invited to submit data by the UK Government on the composition of UK products and exposures reported to it. This abstract identifies the composition of automotive screenwashes currently sold in the UK. **Methods:** The composition of automotive screenwashes was determined from data held on 264 products in the NPIS Product Data Centre. **Results:** Methanol was present in 163 of 264 products (62%), isopropanol in 147 products (56%) and ethylene glycol in 107 products (41%). The majority (71%) of these 264 products contained various combinations of these chemicals. Fifty-eight of 163 products contained <3% w/w methanol, with most of these also containing ethanol (Table 1). Thirty-nine products contained ≥3% methanol but only 38% were co-formulated with ethanol. The exact methanol concentration for 66 products was unknown but all had concentration ranges reported on the product safety datasheet spanning 3%; 46 of these products also contained ethanol. In general, as the concentration of methanol increased, the number of products co-formulated with ethanol decreased. **Conclusion:** In total 163 of 264 screenwash products sold in the UK contain methanol; two thirds of these could potentially contain ≥3% w/w methanol and 61 were co-formulated with ethanol, thereby protecting those ingesting the product from methanol toxicity. If the product contains ≥3% methanol and does not contain ethanol (44 of 105 products), there is the potential for methanol toxicity to occur if ingested.

## 51. Toxicity of oven cleaners as reported to the UK National Poisons Information Service from 2009 to 2014

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**Objective:** Oven cleaning products often contain corrosive substances, typically sodium or potassium hydroxide in concentrations up to 30%. Increasingly, these cleaners are available as aerosols or trigger sprays. This study documents the toxicity of oven cleaners as reported to the UK National Poisons Information Service (NPIS) by doctors and other healthcare workers.

**Methods:** Enquiries to the NPIS regarding oven cleaning products were analysed for the 6 year period January 2009 to December 2014. **Results:** There were 654 enquiries relating to 640 exposures, of which 122 involved children less than 5 years of age. Most exposures (90%) occurred in the home and at least 69% involved sodium or potassium hydroxide-containing oven cleaners. Exposures occurred from ingestion alone (*n* = 234), skin contact alone (*n* = 176), inhalation (*n* = 80), eye contact (*n* = 80) and multiple routes of exposure (*n* = 70). The Poisoning Severity Score was known in 631 of 640 cases: 179 of 640 (28%) patients were asymptomatic (PSS 0), 429 had a PSS 1 (68%), 21 had a PSS of 2 (3%) and 2 had a PSS of 3 (0.3%). Direct ingestion occurred in 112 of 234 patients and 122 claimed to have ingested food “contaminated” with oven cleaner; 54% of the former and 30% of the latter developed features. Overall, the most common features following ingestion alone were nausea and vomiting (*n* = 27), abdominal pain (*n* = 17), pharyngitis (*n* = 13) and numbness or a burning sensation in the mouth (*n* = 12). Of patients exposed dermally 164 of 175 developed features, including burns (*n* = 61), localised skin reactions (*n* = 27), tingling sensation (*n* = 24) at the site of exposure, blistering (*n* = 20) and skin rash (*n* = 19). Inhalation resulted in 73 of 77 patients developing features, including cough (*n* = 23), pharyngitis (*n* = 18) and chest pain (*n* = 12). Eye exposure resulted in features in 66 of 78 cases, including eye pain (*n* = 34), conjunctivitis (*n* = 28) and eye irritation (*n* = 20). **Conclusion:** Most exposures to oven cleaning products, irrespective of the route, resulted in features. These were usually mild but 4% of patients developed moderate or severe features of toxicity.

## 52. Did increasing the number of TOXBASE<sup>®</sup> product entries for liquid laundry detergent capsules increase the number of accesses for these products and reduce the number of telephone enquiries reported to the UK National Poisons Information Service?

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**Objective:** TOXBASE<sup>®</sup> is a poisons information database which can be accessed via the Internet by healthcare professionals. Users are normally hospital departments or general practitioners. This study investigated whether increasing the number of product entries for liquid laundry detergent capsules increased the number of accesses for these products and reduced the number of telephone enquiries to the UK National Poisons Information Service (NPIS). **Methods:** TOXBASE<sup>®</sup> accesses and telephone enquiries to the NPIS regarding liquid laundry detergent capsules were compared over the period January 2008 to September 2015. **Results:** Over the 8 year study period, there were 49,730 TOXBASE<sup>®</sup> accesses and 3565 telephone enquiries (3501 patients) to the UK NPIS regarding liquid laundry detergent capsules. There was a steady increase in the yearly number of TOXBASE<sup>®</sup> accesses between 2008 and 2012 in keeping with the rising popularity of

**Table 1.** Number of TOXBASE<sup>®</sup> entries, accesses and telephone enquiries to the UK NPIS relating to liquid laundry detergent capsules.

Year	TOXBASE <sup>®</sup> entries†	TOXBASE <sup>®</sup> accesses	NPIS telephone enquiries (and exposures)
2008	9	3368	522 (514)
2009	10	4211	501 (490)
2010	10	4737	491 (486)
2011	10	4911	440 (434)
2012	11	5740	433 (422)
2013	54	8532	432 (424)
2014	54	9773	412 (404)
2015	54	11,277*	445* (436*)

Number of TOXBASE<sup>®</sup> entries at end of calendar year.

\*Estimate based on 9 months of data

these products. However, the number of accesses in 2013 was markedly higher than in the previous year (149%). The increase in TOXBASE<sup>®</sup> accesses during 2013 corresponded with the addition of 43 new entries for these products between March and June 2013. The annual number of telephone enquiries (and exposures) decreased between 2008 and 2011, but was steady thereafter. Specifically, there was no corresponding decrease in telephone enquiries to the NPIS in 2013 compared with other years. **Conclusion:** The introduction of 43 new TOXBASE<sup>®</sup> entries for specific liquid laundry detergent capsule variants corresponded with a substantial increase in the number of TOXBASE<sup>®</sup> accesses for these products. However, the increase in the number of accesses to TOXBASE<sup>®</sup> was not associated with a reduction in the number of telephone enquiries to the NPIS regarding liquid laundry detergent capsules.

### 53. Has the International Association for Soaps, Detergents and Maintenance Products (AISE) Product Stewardship Programme had an impact on the number and severity of exposures to liquid laundry detergent capsules reported to the UK National Poisons Information Service (NPIS)?

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**Objective:** More than 1 billion liquid laundry detergent capsules are now sold annually in the UK. Although most of those exposed remain well or develop only minor symptoms, a small proportion develop more serious features. AISE launched a Product Stewardship Programme in December 2012 to reduce the visibility of, and restrict access to, these capsules by small children. Implementation occurred in the UK during the first half of 2013. Our study investigated whether introduction of this Programme led to a reduction in the number and severity of exposures involving liquid laundry detergent capsules reported to the UK NPIS. **Methods:** The number of enquiries, the number of

**Table 1.** Number of liquid laundry detergent capsule enquiries and exposures (and cases PSS  $\geq$  2) reported to the UK NPIS.

Year	Number of enquiries	Number of exposures	Exposures with PSS 2	Exposures with PSS 3	Exposures PSS $\geq$ 2 (%)
2008	522	514	8	2	10 (1.9)
2009	501	490	8	2	10 (2.0)
2010	491	486	9	2	11 (2.3)
2011	440	434	15	1	16 (3.7)
2012	433	422	10	2	12 (2.8)
2013	432	424	7	1	8 (1.9)
2014	412	404	10	0	10 (2.5)
2015	414	403	14	2	16 (4.0)

exposures and the number of more severe cases of exposure (Poisoning Severity Score [PSS]  $\geq$  2) involving liquid laundry detergent capsules were extracted from the NPIS database for the years 2008 to 2015. The Mann-Whitney test (two-tailed) was used to test for statistical differences. **Results:** Although the number of enquiries about, and exposures to, liquid laundry detergent capsules has declined steadily since 2008 (Table 1), there was no significant difference between the annual number of enquiries or exposures reported between the years 2008–2012 when compared to 2014–2015. Furthermore, there was no significant difference in the annual number of cases graded as PSS  $\geq$  2 in 2008–2012 compared to 2014–2015. **Conclusion:** There is no evidence that the Product Stewardship Programme had a statistically significant impact on the number of exposures reported to the UK NPIS or their severity.

### 54. Ocular exposures to bleaches: comparison of severity between sodium hypochlorite and hydrogen peroxide

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**Objective:** Sodium hypochlorite (SH) and hydrogen peroxide (HP) are common ocular exposures. We compared their clinical effects. **Methods:** We queried poison center ocular SH and HP exposure cases from 1 March 2014 to 28 February 2015. The type of data collected included: patient data, route of exposure, dose value and unit, agent name, active ingredients, category code, field of application, packaging, product dilution, eye exposure, circumstances, impacted eye, symptoms present, therapy, medical assessment, symptoms duration, outcome, degree of severity according the Poison Severity Score (PSS). Collected data were analysed in order to identify the most frequent signs and symptoms and to compare the severity of signs after SH and HP based bleach exposure. **Results:** In total data on 69 ocular exposure enquiries were retrieved. The age group distribution was: infant  $n=1$ ; toddlers  $n=23$ , schoolchild  $n=1$ , adult  $n=42$  and unknown  $n=2$ . Most cases (91.3%, 63) were due to SH bleach and 6 (8.7%) to HP. Eye irrigation was performed in all but one case, in which the eyes were washed with warm soapy water prolonging the symptoms for ten days. Clinical effects included: mild irritation (SH  $n=49$ , 25.5%; HP  $n=3$ , 1.6%), moderate irritation (SH  $n=8$ , 4.2%), inflammation (SH  $n=55$ , 28.6%; HP  $n=3$ , 1.6%),



conjunctivitis (SH  $n=6$ , 3.1%; HP  $n=1$ , 0.5%), conjunctivitis aggravated (SH  $n=1$ , 0.5%), pain (SH  $n=18$ , 9.4%; HP  $n=1$ , 0.5%), lacrimation (SH  $n=13$ , 6.8%; HP  $n=1$ , 0.5%), mildly impaired vision (SH  $n=6$ , 3.1%), mild sensation of foreign body (SH  $n=9$ , 4.7%), moderate sensation of foreign body (SH  $n=3$ , 1.6%), severe impaired vision (SH  $n=1$ , 0.5%), mild palpebral oedema (SH  $n=4$ , 2.1%), photophobia (SH  $n=3$ , 1.6%) and corneal abrasion (SH  $n=2$ , 1.0%). PSS ranged from no symptoms in 3 cases (SH  $n=2$ , 2.9%; HP  $n=1$ , 1.5%), minor in 45 cases (SH  $n=40$ , 58%; HP  $n=5$ , 7.2%), moderate in 12 (SH  $n=12$ , 17.4%). PSS was not assignable in 9 cases (SH 13.04%). One adult exposed to a SH bleach reported feeling heaviness of the eye and discomfort for 2 months. Another adult had ocular ulceration following SH bleach exposure; however the eyewash was performed for only one minute. **Conclusion:** The comparison of the PSS assigned in the HP and in the SH groups gave the following results: asymptomatic or minor cases account for the total of HP group without any moderate cases, while 17.4% of the cases were rated as moderate in the SH group. No severe cases were observed in either group.

## 55. Unintended severe poisoning by a modern toilet cleaner: analysis of case reports and product databases for early risk detection

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**Objective:** Given the great variety of household products available, it is difficult to maintain an up-to-date overview of their compositions, particularly with regard to toxicological aspects and their respective poisoning risk. In the field of household chemicals there are increasing numbers of product groups with changing formulations placed on the market. Household products should be safe to use and with respect to foreseeable misuse. A regular evaluation of well-documented cases of poisoning, with specific regard to severe individual cases, as well as a continuously updated overview of the wide range of products available may help to identify risks early and take precautionary measures. **Methods:** Based on the regulations of the German Chemicals Act, physicians who are consulted for treatment or evaluation of sequelae of diseases caused by chemicals are requested to report to the Bundesinstitut für Risikobewertung (BfR; Federal Institute for Risk Assessment) health effects from real or suspected exposures to chemical substances. In addition, submitters of products are obliged to notify formulations of chemical products. A case of severe poisoning in an elderly, demented patient who accidentally drank a strongly acidic toilet cleaner is presented. This is the first reported case of severe poisoning with the newer product group of toilet cleaners for domestic use. This case was the reason to search the product database for new product groups with new risks. **Results:** An 83-year-old patient suffering from severe dementia developed 3rd degree burns to his gastrointestinal tract after ingesting 100 mL of a toilet power cleaner containing 10% hydrochloric acid. There was prolonged hematemesis and necrosis throughout the oesophagus and the stomach. Laboratory tests showed a significant increase in C-reactive protein, metabolic acidosis and a severe decrease in haemoglobin concentration. After parenteral nutrition and symptomatic therapy he stabilized and was discharged in a nursing home/residential care home on day 31. Overview search in the product database revealed that the first power cleaners for consumers

with strongly acidic pH appeared on the German market in 2011. **Conclusion:** Patients with dementia represent a high-risk-group for poisonings. Analysis of reported cases of poisoning can help to early identify special risks. For comprehensive early risk identification, a complete overview of the poisoning situation is required. Product databases containing a wide range of information on the composition and toxicological aspects and their analysis can support identification of risks at an early stage and facilitate improvement of risk management measures.

## 56. Addition of a bittering agent in liquid laundry detergent capsule membranes: is there a tangible ingestion risk decrease? An Italian Poison Control Centre's point of view

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**Objective:** EU 1297/2014 Regulation point 3.3, concerns the addition of a safe concentration of a bittering agent (BA) to liquid laundry detergent capsule (LLDC) hydrosoluble membranes as a deterrent to oral exposure within a maximum time of six seconds. We aimed to verify if the addition of a BA in LLDC membranes can really decrease the risk of paediatric accidental exposures. **Methods:** Three factors were considered concerning the use of a BA within the LLDC's outer membrane: the time required for the membrane's dissolution, the time required for bitter taste perception and the necessary concentration of denatonium benzoate [1] in order to avoid accidents. **Results:** The time required for the LLDC to dissolve when in contact with saliva or wet hands (the most common setting in paediatric exposure cases) is currently still unknown. Therefore, it should be the subject of experimental tests. Bitterness is perceived in the posterior third of the tongue, innervated by the IX cranial nerve terminations. Therefore, bitter taste perception is not as immediate as it is for sweet taste, which is felt on the tip of tongue through the corda tympani. Typically children bite down on the LLDC using their canines, thus piercing the outer membrane almost immediately and causing the detergent to hit the oral mucosa, eyes, and skin causing vomiting, irritation, cough, and other signs and symptoms. Therefore, it seems unlikely that any amount of denatonium benzoate would be adequate to induce a rapid rejection of the LLDC. **Conclusion:** It is widely accepted [2] that adding a BA to a detergent only worsens possible signs and symptoms following ingestion. Therefore, it would be opportune to reconsider whether adding a substance that facilitates vomiting to LLDCs is at all prudent. The addition of a BA does not seem a useful precaution in the absence of adequate experimental studies. Additional data could emerge from the study currently in progress by the European Union in collaboration with Poison Centres.

## References

- [1] Rodgers Jr GC, Tenenbein M. The role of aversive bittering agents in the prevention of pediatric poisonings. *Pediatrics*. 1994;93:68.

- [2] SCCS/1359/10 Scientific Committee on Consumer Safety. Opinion on the potential health risks posed by chemical consumer products resembling food and/or having child-appealing properties. 8.3 pages 21–22.

## 57. Inhalation injury by chlorine generated by mixtures of hypochlorite

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**Objective:** Hypochlorite-containing cleaners may liberate chlorine gas when acidified e.g. by adding an acid sanitary cleaner. Usually these cleaners contain sodium hydroxide or other strong alkalis to stabilise the sodium hypochlorite. We analysed reports to our poisons center concerning inhalation exposure to chlorine liberated from hypochlorite-containing mixtures. **Methods:** A retrospective search of the case database of the poisons center. Cases of human inhalation exposures to chlorine released from mixing hypochlorite as well as human inhalation hypochlorite evaporation alone were analysed. Frequency and symptoms were compared. **Results:** In total 85 cases of human exposures to chlorine from mixtures of hypochlorite and acids (0.8 of 1000 cases) were registered from 2010 to 2015. Of these 94% of exposed patients reported symptoms. In two cases the symptoms were not considered to be caused by the inhalation accident. The most frequent symptoms reported were (percent of symptomatic patients): cough (45%), dyspnea (33%), irritated upper airway (26%), abdominal discomfort (pain, nausea, vomiting) (21%), thoracic pain (20%), irritated eyes (11%), dizziness (8%), and bronchospasm (6%). Further symptoms were malaise, headache, irritated nose, sweating, muscle pain, and others. In 12 patients (14%) the symptoms were graded as moderate severe. The main symptoms in this group were dyspnea (83%), cough, and irritated airway. One third of the patients experienced bronchial obstruction. All symptomatic patients developed symptoms while exposed or shortly after exposure. There were no severe or fatal cases and all symptoms were expected to resolve completely. As hypochlorite-containing cleaners release chlorine-like smelling gases, we additionally analysed inhalation exposures to hypochlorite solutions alone in the same period. There were 42 patients exposed to hypochlorite evaporation alone. Of these 36 of them (86%) had symptoms and in 30 cases these were considered to be caused or possibly be caused by the hypochlorite. The most frequent symptoms were irritated upper airway (33%), nausea or vomiting (30%), cough (23%), irritated eyes (20%), dizziness (13%), dyspnea (10%), headache (8%) and irritated nose (8%). All symptoms were considered mild. **Conclusion:** Despite clear warning on the labels hypochlorite-containing solutions are sometimes mixed with acids. These mixtures cause more pronounced injuries than vapors of hypochlorite solutions alone.

## 58. Acute health problems due to recreational drug use in patients presenting to an urban emergency department in Switzerland

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**Objective:** We describe the frequency and the acute medical problems due to recreational drug use in patients presenting to an emergency department in Switzerland during one year with a focus on novel psychoactive substances. The results were compared with data from the previous year. **Methods:** The study was conducted at the University Hospital of Basel, Switzerland, between October 2014 and September 2015 and within the Euro-DEN project. All cases presenting with acute toxicity due to self-reported acute recreational drug use or with symptoms/signs consistent with acute toxicity were included. Cases of isolated ethanol intoxication were excluded. Drug tests were performed using immunoassays and liquid chromatography-tandem mass spectrometry (LC-MS/MS) to detect novel psychoactive substances. **Results:** During the study period there were 50,624 emergency department attendances of which 210 were directly related to acute toxicity of drugs of abuse. The mean patient age was 33 years and 73% were male. Analytical drug confirmation was available in most (136) cases. Alcohol co-use was reported in 48% of the cases. Use of more than one recreational drug was reported in 24% of the cases and in 34% more than one substance was analytically confirmed. Most presentations were related to cocaine (33%), cannabis (32%), heroin (14%), 3,4-methylenedioxymethamphetamine (MDMA) (7%) and other amphetamines (7%). The most common analytically detected substances were cannabis (33%), cocaine (27%), opioids excluding methadone (19%), benzodiazepines (18%) and amphetamines including MDMA (10%). There were only 2 cases of relatively novel substances (a severe intoxication with para-methoxymethamphetamine (PMMA) in combination with other substances and an intoxication of minor severity with 2,5-dimethoxy-4-propylphenethylamine (2C-P), both self-reported without analytical confirmation). The most frequent symptoms were tachycardia (28%), anxiety (23%), nausea or vomiting (18%) and agitation (17%). Severe complications included 2 fatalities (1 case with MDMA and 1 with heroin), 2 acute myocardial infarctions, seizures (13 cases), and psychosis (6 cases). Most patients (76%) were discharged home, 10% were admitted to intensive care, and 2% were referred to psychiatric care. **Conclusion:** Similar to the prior year, most medical problems related to illicit drugs concerned cocaine and cannabis and mainly included sympathomimetic toxicity and/or psychiatric disorders. We confirm that novel psychoactive substances rarely lead to emergency department consultations (with only two presentations during the study period, similar to the previous year).

## 59. Synthetic cannabinoid receptor agonist (SCRA) toxicity reported to the Victorian Poisons Information Centre

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**Objective:** SCRA have gained prevalence over the last few years due to their marketing as “legal highs”, online availability and challenge to regulate. SCRA toxicosis often results in more severe outcomes than phytocannabinoids and have evolved over time. Exposures and symptoms from SCRA reported to an Australian Poisons Information Centre (PIC) have not been previously published. We aimed to describe the enquiries made to the Victorian

Poisons Information Centre (PIC) regarding SCRA toxicity. **Methods:** A retrospective review of the Victorian PIC electronic enquiry database, using search terms including “synthetic cannabinoids” AND “marijuana”, was performed for the period April 2011 to October 2015. Data collected included patient demographics, reported symptoms, type of caller, intentional or accidental exposure, route of administration, poisoning severity score and product name. **Results:** There were 57 exposures regarding SCRA reported to the Victorian PIC over the study period. Seven (12%) of these involved adolescents (15–19 years old), 44 (77%) were adults (age 20–74) and six (11%) were unrecorded. Fifty-six (99%) cases were intentional and one (1%) accidental use. The majority of exposures were inhalational ( $n=53$ , 93%) and less were ingestions ( $n=4$ , 7%). The poisoning severity scores ranged from none ( $n=9$ , 16%) to mild (40, 70%), moderate ( $n=6$ , 11%) and severe ( $n=2$ , 3%). There were 21 different brands of SCRA products recorded, the commonest being Kronic, Blue Lotus and K2. One of these products, K2, was associated with multiple seizures, decrease in conscious state and cardiac arrest requiring cardiopulmonary resuscitation (CPR) and intubation. The commonest effect was decreased conscious state ( $n=14$ , 25%). Other symptoms included vomiting ( $n=7$ ), agitation ( $n=6$ ), seizures ( $n=6$ ), tachycardia ( $n=4$ ), delirium ( $n=3$ ), dilated pupils ( $n=2$ ), chest pain ( $n=2$ ) and paraesthesia ( $n=1$ ). Symptoms experienced typically manifested within 6 hours. **Conclusion:** SCRA-associated symptoms reported to an Australian PIC were variable but more severe than symptoms previously described with phytocannabinoid use. Continued work is needed to limit harms associated with these products.

## 60. Clinical signs and symptoms in patients poisoned with processed cannabis (Majoon Birjandi) in Eastern Iran

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**Objective:** The pattern of drug abuse varies in different parts of the world.[1–3] Youngsters in the east of Iran abuse processed cannabis which is an ingredient of a traditional pie called Majoon Birjandi (MB).[4] The aim of this study was to evaluate the clinical and paraclinical signs and symptoms in patients poisoned with MB. **Methods:** We designed a cross-sectional descriptive study using a standardized questionnaire administered to all patients with MB poisoning admitted to the toxicology emergency department of the Imam Reza Hospital in Mashhad, Iran from March 2010 to 2011. Information on demographic, medical, psychiatric and electrocardiographic indices and vital signs on admission were collected. **Results:** The study included 37 patients with an average age of 23 years, 34 of whom were men and three women. Patients had consumed a mean (SD, minimum-maximum) 1.3 (0.8, 0.5–3) pies. All patients were positive for tetrahydrocannabinol (THC) by urinary immunoassay. Common symptoms reported according to frequency were sore throat (92%) followed by dry mouth (91%), flushing (81%), panic (73%), vertigo (73%), conjunctivitis (60%) and agitation (62%). Most patients had mydriasis and this was statistically related to QRS widening ( $p=0.04$ ). In addition ten patients presented with decreased level of consciousness. Onset of signs after ingestion of MB was longer than expected with cannabis and effects were of longer duration. **Conclusion:** It appears that the major ingredient of MB is cannabis. In comparison to the literature related to smoking cannabis,

clinical manifestations of ingesting MB appear later and last longer.

## References

- [1] Mehrpour O, Sezavar SV. Diagnostic imaging in body packers. *Mayo Clin Proc.* 2012;87:e53–e54.
- [2] Karrari P, Mehrpour O, Balali-Mood M. Iranian Crystal: a misunderstanding of the crystal-meth. *J Res Med Sci.* 2012;17:203–204.
- [3] Zavar A, Afshari R, Alidoust M, et al. Curriculum development in regard to illicit drug abuse. *FMEJ.* 2012;2:31–36.
- [4] Mehrpour O, Karrari P, Afshari R. Recreational use and overdose of ingested processed cannabis (Majoon Birjandi) in the eastern Iran. *Hum Exp Toxicol.* 2012;31:1188–1189.

## 61. An unhappy end for a party involving *Datura stramonium* and other abuse drugs

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**Objective:** Cases involving *Datura stramonium* comprise 1.8% of all toxic plant exposures reported to our center. In summer 2011 we registered three cases involving *Datura stramonium* and drugs of abuse which occurred at a party in an abandoned farmhouse. Three friends assumed they had ingested amphetamines (“speed”), ethanol and an unknown dose of a beverage made from *Datura stramonium* seeds offered at the party. **Case report:** Case 1: A 20-year-old man was admitted to an emergency department at 6 am, with a Glasgow Coma Scale of 9, agitation, hyperthermia, generalized rigidity, tremors and bilateral mydriasis. Neostigmine and diazepam were administered, and agitation and tremors decreased. Hospital screening urine drug tests were negative, and blood ethanol was 1.67 g/L. He presented with sinus tachycardia, hypertension, dry mouth and hot flushed skin. Haematology, renal function and creatine phosphokinase were normal. Treatment was symptomatic and supportive. His signs resolved and he was discharged on day 2. Comprehensive toxicological screening for psychoactive substances and drugs of abuse was performed including ethanol and volatile analysis by head-space-gas chromatography with flame ionization detector (HS-GC-FID), enzyme immunoassay, and an extensive analysis in blood by high-performance liquid chromatography with diode-array detection (HPLC-DAD), gas chromatography-mass spectrometry (GC-MS), and liquid chromatography-tandem mass spectrometry (LC-MS/MS). Results were negative. Cases 2 and 3: Two males, 17 and 18-years-old, were found dead on waste ground after attending the same party. Their bodies showed obvious signs of dehydration. Forensic examination determined the time of death as 5 pm on the same day patient 1 was admitted. The maximum temperature that day was around 40 °C. The 18-year-old was seen naked, walking aimlessly at 4 pm and refused any help. At 6 pm he was found dead. Autopsies were performed the following day. No signs of violence were found. Urine, blood, gastric contents, liver, brain and kidney were submitted for analysis. Toxicological results in case 2 were: atropine detected in brain, stomach, liver, blood and urine, while scopolamine was only detected in urine. Amphetamine, 3,4-methylenedioxymethamphetamine (MDMA), and alcohol were found in different biological matrices. In case 3

atropine and scopolamine were found in stomach contents, while only atropine was found in liver and urine. Amphetamine, MDMA, tetrahydrocannabinol (THC) and alcohol were found in different biological matrices. **Conclusion:** Despite the low percentage of *Datura stramonium* consults recorded by our PCC, poisonings and fatalities related to this plant have been detected.

## 62. Not your regular high: Potentially lethal cardiac dysrhythmias caused by loperamide

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**Objective:** Loperamide, a non-prescription anti-diarrheal agent, is a peripheral mu-opioid receptor agonist that is excluded from the blood-brain barrier by P-glycoprotein at therapeutic doses, but in overdose it penetrates the central nervous system (CNS). We report cardiac conduction abnormalities and dysrhythmias after ingestion of a recreational supra-therapeutic dose of loperamide with laboratory confirmation. **Case report:** A 48-year-old woman with a history of alcohol and benzodiazepine abuse presented with somnolence, weakness and slurred speech. She had been taking 20–40 tablets of 2 mg loperamide 1–2 times/day for weeks with clonazepam and whiskey. Vital signs were blood pressure (BP) 124/90 mmHg, pulse 88/min, respiratory rate 20/min, temperature 36.9°C and oxygen saturations 100% on room air. Glucose was 6.4 mmol/L. An electrocardiogram (ECG) approximately ten minutes later showed a ventricular rate of 56/min, QRS 164 ms, QTc 571 ms with no discernible P waves. Lactate was 3.5 mmol/L and potassium was 6.2 mEq/L. Laboratory findings were an anion gap of 20, ethanol concentration 3.9 mmol/L, creatinine 203 µmol/L, and loperamide concentration 210 ng/mL (average therapeutic <10 ng/mL). She became hypotensive, but responded to fluids. Following treatment for hyperkalemia with 2 g calcium gluconate, insulin 10 Units, dextrose 50%, and hyper-tonic sodium bicarbonate, a repeat ECG showed a ventricular rate of 66/min, QRS 156 ms, QTc 603 ms. Magnesium was given and pacer pads were placed. During the infusion of magnesium her BP fell to 92/58 mmHg with pulse 54/min, respiration rate 14/min, and saturations 97% so the infusion was stopped. The ECG after the magnesium infusion had a ventricular rate of 51/min, QRS of 134 ms, and QTc 570 ms. In the ICU she had multiple runs of non-sustained ventricular tachycardia. She improved over the next 48 hours, was transferred to a floor bed but on day four of hospitalization left against medical advice. At that time her ECG showed sinus tachycardia, QRS 82 ms and QTc 460 ms. **Conclusion:** Loperamide produces both QRS and QT prolongation at supra-therapeutic dosing. A blood loperamide concentration of 210 ng/mL is among the highest reported. Supra-therapeutic dosing of loperamide is promoted on multiple drug-use websites and online forums as a treatment for opioid withdrawal and a possible methadone alternative. With the current epidemic of prescription opioid abuse, toxicity related to loperamide, an opioid agonist that is readily available over-the-counter, is occurring more frequently. It is important for clinicians to be aware of the potentially life-threatening toxicity related to loperamide abuse in order to provide proper diagnosis, management and patient education.

## 63. Inhalational heroin resulting in acute cardiomyopathy and sensorineural hearing loss

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**Objective:** To describe what we believe to be the first reported case of inhalational heroin use resulting in both opioid-induced sensorineural hearing loss and heroin-induced acute cardiomyopathy. Opioid-induced sensorineural hearing loss has been reported in numerous case reports. The mechanism of ototoxicity is unknown and most patients make a complete neurologic recovery. Heroin-induced acute cardiomyopathy has been rarely reported and may feature near global myocardial hypokinesia and reduced ejection fraction. Patients may recover some heart function but recovery is typically incomplete. **Case report:** A 15-year-old male was admitted to the intensive care unit (ICU) after an overdose involving both oral alprazolam and inhalation of heroin. The patient's mother found him unresponsive the morning of presentation. On arrival the patient was given naloxone without response and upon arrival at the Emergency Department (ED) he was endotracheally intubated for airway protection. Initial vital signs were temperature 36.3°C, heart rate 123 beats/min, respiratory rate 8/min, blood pressure (BP) 109/64 mmHg and oxygen saturations 99% on room air. Shortly after intubation heart rate normalized to 89 and BP dropped to 77/48 mmHg. Physical examination was remarkable only for decreased mentation, pinpoint pupils and bradypnea. Initial laboratory work up showed an elevated creatinine of 2.3 mg/dL, lactate 8 mmol/L, aspartate transaminase (AST) 1103 IU/L with negative acetaminophen, creatine kinase (CK) 533 IU/L and troponin 1.56 ng/mL. Urine drug screen was positive for benzodiazepines, tetrahydrocannabinol (THC) and opiates. Electrocardiogram (ECG) showed a right bundle branch block and Brugada-like patterns. CK and troponin peaked the next day at 21,800 IU/L and 12.9 ng/mL, respectively. An echocardiogram the same day showed hypokinesia of the entire myocardium except for the basal and mid-posterolateral wall, the ejection fraction (EF) was about 30%. On hospital day 2 the patient was extubated and complained of hearing difficulty which was confirmed as moderate bilateral sensorineural hearing loss on audiology testing. Over the course of the next 48 hours there was resolution of cardiomyopathy as evident by an echocardiogram with an EF of 63% without dyskinesia apparent. As for the hearing loss, the patient was placed on a course of oral steroids and had significant improvement by the time of discharge. **Conclusion:** We report what we believe to be the first case of simultaneous opioid-induced sensorineural hearing loss and heroin-induced acute cardiomyopathy. Both the hearing loss and cardiomyopathy improved over a period of days.

## 64. A fatal case of acute clenbuterol poisoning

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**Objective:** Clenbuterol is a long acting beta-2-adrenergic agonist with anabolic, lipolytic and sympathomimetic properties, used mostly in veterinary practice. Its effects are also coveted by some body builders. We report the death of an adult after intake of an

acute overdose. **Case report:** A 36-year-old body builder using various anabolic substances ingested up to 50 tablets of clenbuterol of an unknown strength. His past medical history included a mechanical aortic valve inserted during his youth, subsequent warfarin treatment with low compliance and medication with sertraline and gabapentin. Shortly after the drug intake he was found in general convulsions without spontaneous breathing. Cardiopulmonary resuscitation was started immediately by his girlfriend. Upon arrival of the ambulance electrocardiogram showed ventricular fibrillations. He was intubated by the ambulance personnel and received multiple defibrillations during transport to hospital. On admission to the emergency room resuscitation was continued including repeated defibrillations, bolus doses of amiodarone (450 mg in total), repeated doses of adrenaline, magnesium and norepinephrine infusion. The patient was temporally stabilized and forced cooling was initiated prophylactically against hypoxic brain injury. Laboratory tests showed an elevated troponin T concentration of 84 ng/L. Lactate was 7.6 mmol/L, glucose 9.4 mmol/L and leucocytes  $26.5 \times 10^9/L$ . The potassium value was not interpretable due to test tube hemolysis. During the following hour the patient had reoccurring episodes of ventricular tachycardia including suspected torsades de pointes. Cardiac index was 2.63 L/min/m<sup>2</sup> (normal range 2.8–4.2 L/min/m<sup>2</sup>) and blood pressure 60/40 mmHg. Treatment with intravenous lipid emulsion was tried without positive effect. Further resuscitation efforts were considered futile and were withheld approximately four hours after the debut of symptoms. Autopsy revealed myocardial ischemia with a pale anterior wall of the left chamber. The patient's mechanical aortic valve was without any flaws and the suture line intact. Clenbuterol ingestion was verified by post mortem analysis (2 ng/g blood). The cause of death was stated as acute cardiac ischemia. **Conclusion:** Clenbuterol overdose is known to cause massive catecholamine release and subsequent risk of myocardial ischemia and arrhythmias, symptoms our patient presented in a pronounced and malignant way.[1] Takotsubo cardiomyopathy may also be a mechanism for acute heart failure in such cases; an echocardiogram may confirm this condition. Treatment attempts with catecholamines intravenously will probably exacerbate the situation.

## Reference

- [1] Huckins DS, Lemons MF. Myocardial ischemia associated with clenbuterol abuse: report of two cases. *J Emerg Med.* 2013;44:444–449.

## 65. Clinical features and outcomes in a case series of 549 MDMA-related acute toxicity presentations reported to the European Drug Emergencies Network (Euro-DEN) project over 15 months

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**Objective:** Although MDMA (3,4-methylenedioxyamphetamine, ecstasy) is a familiar drug to clinical toxicologists and poisons centres, there are only small published series of acute MDMA toxicity. The aim of this study is to describe the demographics and clinical features of acute MDMA toxicity presentations to the Euro-DEN project over a 15-month period. **Methods:** Data was collected from 16 sentinel centres in 10 European countries (Denmark, Estonia, France, Germany, Ireland, Norway, Poland, Spain, Switzerland, the UK) using the Euro-DEN minimum dataset for 15 months (1 October 2013 to 31 December 2014).[1] The following data was extracted: age and gender, self-reported drugs used, clinical features, initial disposition from the emergency department (ED), length of hospital stay and outcome. **Results:** Of the 6747 presentations to Euro-DEN over this 15 month period, 549 (8.1%) involved the use of MDMA prior to presentation. The proportion of presentations to each Euro-DEN centre that involved MDMA varied from 0 to 16.7%. The majority of presentations involving MDMA were male (70.5%) and the mean  $\pm$ SD age was  $24.7 \pm 6.6$  years. The mean  $\pm$ SD number of drugs (excluding ethanol) per presentation was  $1.9 \pm 0.7$ ; the top 3 co-ingestants were cocaine (124, 23%), cannabis (71, 13%) and gammahydroxybutyrate/gammabutyrolactone (GBH/GBL) (44, 8%); these varied across sites reflecting the different recreational drug use patterns. The most commonly reported clinical features were agitation/aggression (174 presentations, 31.7%), anxiety (131, 23.9%), palpitations (69, 12.6%) and chest pain (55, 10.0%). Hyperthermia (temperature  $\geq 39^\circ\text{C}$ ) was recorded in 16 (2.9%) patients. There were 2 deaths and both occurred in individuals with hyperthermia (temperatures on presentation of  $40.5^\circ\text{C}$  and  $41.8^\circ\text{C}$ ). The median length of stay was 3 hours 43 minutes (IQR 1h 57m to 5h 37m). The majority (323, 58.8%) of patients were medically discharged from the ED, 91 patients (16.6%) self-discharged, 25 (4.6%) were admitted to critical care, 14 (2.6%) were admitted to a psychiatric ward and 89 (16.2%) to another ward. **Conclusion:** In this large series of presentations with acute MDMA toxicity, clinical features were stimulant/sympathomimetic in nature. There were two deaths and these occurred in patients with hyperthermia on presentation. The overall outcome was good with the majority of patients discharged from the ED.

## Reference

- [1] Wood DM, Heyerdahl F, Yates CB, et al. The European Drug Emergencies Network (Euro-DEN). *Clin Toxicol (Phila).* 2014;52:239–241.

## 66. The impact of legislative control of methylphenidate-based novel psychoactive substances on recreational drug-related admissions to the Royal Infirmary of Edinburgh

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**Objective:** In recent years the number of patients admitted to hospital following the use of novel psychoactive substances (NPS) has increased substantially. Methylphenidate-based NPS are associated with many adverse effects including paranoia, violent behaviour, bacterial infection risk and death.[1] In an effort to reduce harm, methylphenidate-based NPS were controlled by the UK government under the Misuse of Drugs Act 1971 (Temporary Class Drug) Order on 10 April 2015. The aim was to assess whether the legislative control of these substances had an effect on recreational drug-related admissions to a Scottish teaching hospital. **Methods:** Data for all recreational drug-related admissions to the Royal Infirmary of Edinburgh, from 10 October 2014 to 9 October 2015 were obtained and analysed. All data were obtained prospectively, except for the non-NPS recreational drug data in the pre-control group, which were obtained retrospectively from patient records. Both single substance and polysubstance use was included. Statistical analysis was performed by a two-tailed Fisher's exact test. **Results:** There were 290 recreational drug-related admissions in the 6 months before and 263 admissions in the 6 months after the control of methylphenidate-based NPS. Admissions associated with NPS decreased from 192 (66% of total admissions) pre-control to 135 (52%) post-control. Not all patients were able to report which NPS they had used but reported methylphenidate-NPS related admissions reduced significantly following legislation, with 88 in the pre-control period compared to 8 post-control ( $p < 0.0001$ ). In contrast, synthetic cannabinoid usage increased from 22 patients before, to 60 patients after legislation ( $p < 0.0001$ ). A similar pattern was observed with stimulant NPS (methiopropamine and cathinones), 12 pre-control versus 27 post-control. Hospital admissions associated with opioid (heroin, dihydrocodeine, methadone) toxicity also increased from 83 (29%) to 109 (41%) after methylphenidate-based NPS control ( $p = 0.002$ ). The opioid increase was most apparent immediately after the legislation changed with admissions increasing from 27 to 49 cases in the two months before and after the change. A similar pattern was observed for benzodiazepine admissions, increasing from 17 to 37 cases in the 2 months before and after legislation. **Conclusion:** This study demonstrates that the control of methylphenidate-based NPS was associated with an immediate reduction in hospital admissions with toxicity. However, there was a sharp increase in opioid admissions immediately after legislation and a steady increase in the use of other NPS over the following 6-month period.

## Reference

- [1] The Home Office: Circular 015/2015 temporary control of 5 methylphenidate-based NPS; [cited 2015 Nov 21]. Available at: <https://www.gov.uk/government/publications/circular-0152015-temporary-control-of-5-methylphenidate-based-nps/circular-015-2015-temporary-control-of-5-methylphenidate-based-nps>

## 67. Drugs of abuse used by patients presenting to the Emergency Department over a one year period

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**Objective:** To report the epidemiologic characteristics of drug users and the prevalence of substances used. **Methods:**

**Table 1.** The drugs taken in cases reported to the Greek PIC ( $n = 121$ ).

Drugs of abuse	Number of cases	In combination with:	Number of cases
Opioids-heroin	58	Alcohol	3
Heroin in isolation	11	Psychoactive	2
		Cocaine	7
		Benzodiazepines	23
		Methadone	4
		Multiple drugs	8
Cocaine	13	Alcohol	1
Cocaine in isolation	4	Benzodiazepines	2
		Cannabis	2
		Multiple drugs	4
Cannabis	17	Alcohol	1
Cannabis in isolation	9	Benzodiazepines	2
		Amphetamines	1
		Multiple	4
Amphetamines	15	Multiple drugs	6
Amphetamines in isolation	9		
LSD	6	Multiple drugs	2
LSD in isolation	4		
Other drugs			
Synthetic cannabinoids	4		
Tai kai	2		
Sisa	2		
Poppers	1		
Unknown	3		

A retrospective study based on the database of the Greek Poison Information Center (PIC) was conducted, regarding patients who presented to emergency departments because of drug abuse from 1 October 2014 to 30 September 2015. Collaboration between the PIC and Emergency Departments was necessary because of the severity of poisoning. Age, gender, origin, symptoms, type of substances and combinations were recorded. **Results:** The National Statistical Service of Greece recorded 2293 admissions due to substance dependence, which accounts for approximately 1% of total admissions. Referral to the PIC was necessary for 121 patients in critical condition. Mean age of the patients was 32.3 years, 75.2% were males, including 5 children aged 9–15 years old. In total 36.4% of cases occurred in hospitals in Athens. Furthermore 7 patients were body stuffers. The substances used are shown in Table 1. The most common combinations involved benzodiazepines (34.7%) and alcohol (12.4%).[1] Additionally 1074 patients were reported with benzodiazepine abuse; it was uncertain whether they were drug-dependent or had attempted suicide. Central nervous system (CNS) effects were recorded in 71 patients while 23 of them were comatose and 4 were intubated. In 20 cases cardiovascular symptoms presented. In addition 37 had visual impairment and one had acute renal failure. In 43 patients naloxone or flumazenil was given. There were no deaths in the PIC cases and 20 (all males) in the Statistical Service records. **Conclusion:** Heroin and cocaine use is the major cause of poisoning needing hospitalization followed by cannabis and amphetamines, while new synthetic cannabinoids, self-made mixtures and lysergic acid diethylamide (LSD) are less frequent.

## Reference

- [1] Jones JD, Mogali S, Come SD. Polydrug abuse: a review of opioid and benzodiazepine combination use. *Drug Alcohol Depend.* 2012;125:8–18.

## 68. Chest pain associated with recreational use of cocaine and mephedrone: should we be asking patients about use?

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**Objective:** Previous studies from the US and Spain involving analysis of urine samples have found cocaine metabolites in up to 25% of all patients with acute coronary syndrome (ACS).[1] The aim of this study was to determine the prevalence of cocaine and mephedrone use in patients presenting with suspected ACS by analysis of blood samples and whether a history of drug use was obtained by the attending clinician. **Methods:** Potential ACS cases were prospectively identified from the hospital computerised blood test system of one inner-city London teaching hospital. Patients over 18 years old presenting to the Emergency Department during September 2014 who had a blood test for troponin T were included. The blood samples taken were also subsequently analysed by liquid chromatography-tandem mass-spectrometry (LC-MS/MS) for the presence of cocaine, mephedrone and their metabolites. Data on patient demographics, clinical presentation and troponin/creatinine results were obtained from the medical records. **Results:** In total 384 patients met the inclusion criteria (267 males, 117 females); the mean  $\pm$  SD (range) age was  $59.2 \pm 17.1$  (19–98) years. Of these, 7 (2%) male patients had detectable drugs in the blood sample (5 cocaine and metabolites, 1 cocaine metabolites, 1 mephedrone); their mean age was lower than those where drugs were not detected ( $37.9 \pm 11.8$  years compared to  $59.6 \pm 17.0$  years,  $p < 0.001$ ). A history of cocaine/mephedrone use was documented by the attending clinician in 4 (57%) of these 7 cases; 1 (14%) denied drug use and 2 (29%) had no documentation of use. **Conclusion:** A small minority of patients presenting with suspected ACS had analytical confirmation of cocaine or mephedrone use prior to the onset of chest pain and a history of drug use was only documented in just over half of the patients who had drugs detected. It is important that clinicians ask patients presenting with chest pain about drug use prior to presentation. Patients with positive samples were younger, in keeping with past studies but the overall proportion of positive samples were much lower, this is likely to be because previous studies have looked at cocaine metabolites rather than parent drug.[1] Further work needs to be done to determine the true incidence of sympathomimetic drug-related ACS in larger cohorts.

### Reference

- [1] Hollander JE, Todd KH, Green G, et al. Chest pain associated with cocaine: an assessment of prevalence in suburban and urban emergency departments. *Ann Emerg Med.* 1995;26:671–676.

## 69. “Mâajoune” preparations: the most legendary confections of cannabis with other substances of abuse in Morocco

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**Objective:** Traditional abuse of cannabis as a preparation called “Mâajoune” in Morocco is common. It contains cannabis, as the main ingredient, and other substances such as atropine hallucinogenic plants, poppy seeds and psychotropic drugs depending on the region where it is made. It was the most common substance of abuse incriminated in the drug poisoning cases reported to the Poison Control and Pharmacovigilance Centre of Morocco (CAPM).[1] The aim of our study was to analyze the aspects of consumption of this mixture over the past two years. **Methods:** A retrospective study from January 2013 to December 2014 of all cases of poisoning by “Mâajoune” reported to the CAPM. The data included circumstances of poisoning, sex, age distribution and symptomatology. The age classification used was the International Programme on Chemical Safety classification. We used a logistic regression model to determine the risk factors of hospitalization. **Results:** “Mâajoune” was the most drug of abuse responsible for poisoning (49.9% of all substance abuse intoxications). The average age was  $19.6 \pm 8.4$  years. The most affected age group was adults (45.6%) followed by adolescents (32.6%) and patients aged less than 15 years (infant, toddler and children 22.1%). The sex ratio (M/F) was 3.6. Addictive circumstance was the most frequent (66.4%) followed by accidents (30.4%). In 85.6% of the cases, patients were symptomatic. The dominating clinical signs were gastrointestinal (40.3%) and neurological (38.4%). The risk factor for hospitalization was age less than 15 years ( $p = 0.01$ , OR 1.6). **Conclusion:** The consequence of the trivialization of “Mâajoune” consumption in Morocco is the increase in poisoning cases in young addicts but also accidental poisoning in children. An awareness program in schools and through the media is needed to address this scourge.

### Reference

- [1] Chaoui H, Rhalem N, Semlali I, et al. Poisoning by substances of abuse in Morocco: Moroccan poison control center data (1980 to 2009) and risks factors for death. *Rev Res J.* 2014;3:1–8.

## 70. Epidemiology and clinical picture of hashish oil poisoning in Slovenia

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**Objective:** Hashish oil is a dark, viscous organic substance produced from the resin collected from the flowering tops of *Cannabis sativa* plants. It contains varying concentrations of tetrahydrocannabinol (THC) up to 50%. Despite the prohibition, abuse of THC is widespread among the Slovenian population. The use of hashish oil is propagated for medicinal purposes, as it is believed to be generally beneficial. The aim of the study was to evaluate the epidemiology of hashish oil poisoning in Ljubljana,

Slovenia. **Methods:** In this retrospective study we analyzed the clinical presentation of adult patients poisoned with hashish oil who were treated in the past 7 years (2008–2014) at the University Medical Centre Ljubljana (UMCL), the primary city hospital for the Slovenian capital city of Ljubljana, serving a population of 600,000 inhabitants. We analysed the demographic data, clinical picture and treatment of hashish oil-poisoned patients. **Results:** Over the study period 19 adult patients poisoned with hashish oil were hospitalized in the UMCL (2008  $n=1$ , 2009  $n=1$ , 2011  $n=1$ , 2012  $n=2$ , 2013  $n=4$ , 2014  $n=10$ ). Patients poisoned with hashish oil were older than other cannabis users (mean age 47.4 years) and they did not combine hashish oil with other illegal substances or alcohol. Circumstances include 9/19 patients who consumed hashish oil in anticipation of symptomatic relief or resolution of their illness (e.g. malignancies, gout, arterial hypertension) or to achieve relaxation (5/19). On presentation clinical signs included drowsiness (10/19), slowness (5/19), malaise (4/19), confusion (3/19), anxiety (3/19), hallucinations (2/19), distorted perception of the body or surroundings (2/19) and euphoria (2/19). Patients often felt nausea (9/19) and vomited (3/19). They also had dysarthria (5/19), mydriasis (4/19), diaphoresis (3/19), tremor (2/19) and muscle spasms (2/19). They were tachycardic (7/19) or bradycardic (6/19). Most patients (16/19) needed active treatment, mostly parenteral hydration (11/19), benzodiazepines (5/19) and antiemetics (1/19). Decontamination with activated charcoal was performed in 2 patients; 11/19 patients were hospitalized for a brief period (1–2 days). All of them survived poisoning with hashish oil. **Conclusion:** The frequency of hashish oil poisoning has increased in Slovenia during the last few years. Accordingly, urine THC screening is becoming essential in older patients with unexplained altered consciousness and nausea to confirm diagnosis.

## 71. Online survey on prescription medicine misuse: what is the evidence for prescription opioid misuse in Singapore?

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**Objective:** Prescription opioid misuse has been shown to be a serious public health issue in the US and Europe.[1,2] Our objective was to establish the awareness of a range of prescription opioids and the prevalence of their misuse (defined as use without a doctor's prescription or for any reason other than what was recommended by your doctor) in Singapore where there is little data available. **Methods:** An online survey administered through a market research company in September 2015. Basic demographic data (gender, age, race, employment status) and data on whether individuals had heard of a range of opioid drugs and if so, whether they had ever misused them were collected. **Results:** One thousand respondents completed the survey: 500 (50.0%) male, 499 (49.9%) female, and 1 (0.1%) transgender; median (IQR) age was 35 (29–45) years; 82.5% were Chinese, 8.2% Indian, 5.4% Malay, 0.8% Eurasian and 3.1% other race/ethnicity. Most were employed (85.4%), 11.3% unemployed and 3.3% were students. Codeine was the individual drug that most respondents had heard of (30.2%), see Table 1; 437 (43.7%) respondents had heard

**Table 1.** Number (%) of respondents of an online survey who had heard of and reported life-time misuse of prescription opioids.

Drug Name	Number (%) of respondents who had heard of the drug	Number (%) of respondents who had heard of the drug and reported lifetime misuse
Codeine	302 (30.2%)	23 (7.6%)
Dhasedyl <sup>®</sup> (codeine, ephedrine and promethazine)	175 (17.5%)	16 (9.1%)
Panadeine <sup>®</sup> (codeine and paracetamol)	175 (17.5%)	15 (8.6%)
Tramadol <sup>®</sup>	136 (13.6%)	11 (8.1%)
Procodin <sup>®</sup> (codeine and promethazine)	125 (12.5%)	4 (3.2%)

of any codeine containing product and 459 (45.9%) had heard of any opioid. The reported lifetime misuse of any codeine-containing product was 40 (9.2%) and any prescription opioid was 47 (10.2%). **Conclusion:** This pilot study suggests prescription opioid misuse occurs in Singapore. Further work is needed to understand its true extent, reasons for misuse, and sources of the drugs to help develop public health initiatives to tackle this issue.

## References

- [1] Birnbaum HG, White AG, Schiller M, et al. Societal costs of prescription opioid abuse, dependence, and misuse in the USA. *Pain Med.* 2011;12:657–667.
- [2] Amie Shei A, Hirst M, Kirson NY, et al. Estimating the healthcare burden of prescription opioid abuse in five European countries. *Clinicoecon Outcomes Res.* 2015;7:477–488.

## 72. Acute neurotoxicity of bath salts combining 3,4-methylenedioxypropylvalerone and mephedrone in the rat

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**Objective:** Synthetic cathinones, beta-keto-amphetamine derivatives, are new psychoactive and stimulant substances with exponentially increasing use in the last 10 years. “Bath salts”, often sold legally, contain mixtures of several cathinones such as 3,4-methylenedioxypropylvalerone (MDPV) and mephedrone (4MMC). Toxicity of a combination of two cathinones, mimicking their real use in humans, has never been studied. Our objective was to investigate possible synergy of MDPV/4MMC combination on their stimulant effects in the Sprague-Dawley rat and analyze their mechanisms of interaction. **Methods:** MDPV and 4MMC were synthesized in our laboratory. We studied the effect of a MDPV/4MMC mixture (administered by the intragastric route) on rat locomotor activity in an open-field using video-tapping. Plasma concentrations of MDPV, 4MMC and their 3 major metabolites were measured using liquid chromatography coupled to mass spectrometry high-resolution. Brain monoamine concentrations were determined using high-performance liquid chromatography coupled to fluorometry. For each animal and each time, we calculated the difference between the parameter value at that time



and baseline and the area under the curve of its time course. Comparisons were performed using two-way ANOVA followed by post-tests using Bonferroni correction. Pharmacokinetics (PK) was modeled and parameters calculated using WinNonlin® software. **Results:** MDPV (3 mg/kg)/4MMC (30 mg/kg) combination was responsible for a significant increase in rat locomotor activity in comparison to saline, MDPV and 4MMC alone ( $p=0.02$ ), with a synergic interaction between the two drugs. 4MMC PK was not altered in the presence of MDPV while MDPV absorption was reduced in the presence of 4MMC without significant modifications in its half-life and clearance. The neurochemical study revealed significant increase in dopamine and serotonin but not in norepinephrine concentrations in the prefrontal cortex, when combining both drugs in comparison to each drug administered separately. **Conclusion:** A MDPV/4MMC mixture as found in "bath salts" significantly increases locomotor activity in rats in comparison to each substance administered alone. Mechanisms of interaction include significant decrease in MDPV gastrointestinal absorption and significant increase in monoamine reuptake inhibition in the brain with reinforcement of both the dopaminergic and serotonergic profiles. However, further investigations at the level of gastrointestinal transporters and monoamine transporters are required.

### 73. Substance abuse among medical students in Maribor, Slovenia

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**Objective:** There is little information about how familiar future physicians in Slovenia are with the abuse of substances. Our aim was to investigate lifetime abuse of drugs and illicit drugs among medical students at the Faculty of Medicine in Maribor, Slovenia. **Methods:** An online anonymous self-administered questionnaire was developed. Through email and the faculty website, 645 students (from 1st to 6th year of study) were invited to participate in completing the questionnaire. Questions were related to age, gender, year of study, other basic demographic information as well as to consumption of alcohol, cigarettes, cannabis, synthetic cannabinoids, alkyl nitrites, inhalants, amphetamines, cocaine, lysergic acid diethylamide (LSD), magic mushrooms, heroin, gamma-hydroxybutyrate (GHB) and mephedrone. The data was anonymously collected and stored on servers of an independent survey provider. The results were descriptively evaluated. **Results:** In total 288 out of 645 (45%) students responded. From the respondents, 69% were females and 31% males; which closely represents the ratio of female to male students at our faculty. The mean age of students participating in the study was  $22.0 \pm 2.2$  years. Of the respondents 70% had used a substance for abuse at some point. Most frequent drugs of abuse were alcohol and cannabis, with a lifetime prevalence of 67% and 40%, respectively; 8% of students were smokers, 11% reported smoking occasionally, 65% were non-smokers and 16% did not answer the question on smoking. Magic mushrooms had been used by 8%, whereas 7% of students used amphetamines and 3% cocaine. There was a higher prevalence of consumption among male compared to female students (75% versus 68%, respectively). Also, a higher substance use in 6th compared to 1st year students was noted (88% versus 66%, respectively). **Conclusion:** In comparison with similar studies on medical students, we report lower alcohol consumption, lower tobacco usage and lower cannabis consumption in our students; however, higher consumption of hallucinogens was observed.[1–3] Further investigations on frequency and reasons for abusing substances are required.

### References

- [1] Roncero C, Egido A, Rodríguez-Cintas L, et al. Substance use among medical students: a Literature Review 1988–2013. *Actas Esp Psiquiatr.* 2015;43:109–121.
- [2] Višnjić A, Jović S, Grbeša G. Alcohol consumption among students – a cross-sectional study at three largest universities in Serbia. *Srp Arh Celok Lek.* 2015;143:301–308.
- [3] Voigt K, Twork S, Mittag D, et al. Consumption of alcohol, cigarettes and illegal substances among physicians and medical students in Brandenburg and Saxony (Germany). *BMC Health Serv Res.* 2009;9:219.

### 74. Abuse of synthetic cannabinoids in Israel: reports to the National Poison Information Center 2010–2014

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**Objective:** Synthetic cannabinoid receptor agonists comprise a large family of structurally unrelated substances marketed as abusable designer drugs. Since 2011, many synthetic cannabinoids have been included in Israel's controlled substance act, but there is little information about the epidemiology of synthetic cannabinoid abuse in Israel. We therefore surveyed demographic and clinical characteristics of synthetic cannabinoid users reported to the Israel Poison Information Center. **Methods:** We searched the Israel Poison Information Center electronic database for cases of synthetic cannabinoid use and withdrawal syndrome between January 2010 (first report of synthetic cannabinoid use) and December 2014. Callers' data and patients' demographic and clinical data were extracted and subjected to descriptive analysis. Laboratory identification was not done since at present there is no analytical laboratory in Israel performing analyses of synthetic cannabinoids in body fluids. Therefore, the identification of the culprit was based on self-report by the users or their escorts according to the substance description and common street names. **Results:** Over the study period 107 cases of synthetic cannabinoid use were reported to the Israel Poison Information Center. The number of reports increased consistently each year, starting with 10 in 2010 and reaching 67 in 2014. Most of the callers (93%) were healthcare professionals. Users were predominantly young males (median age 22 years, range 12–51 years; 84% males). In most cases (93%), the substance was smoked. The most frequent clinical manifestations were gastrointestinal (nausea or vomiting 35%, diarrhea 10%), neuro-psychiatric (agitation 23%, psychoses or hallucinations 15%, headache 12.5%, drowsiness 9%, seizures 5%) and cardiovascular (sinus tachycardia 22%, supra-ventricular tachyarrhythmias 3%, chest pain 10%, bradycardia 9%, hypertension 4%). Two percent had acute kidney injury. Symptoms were of moderate severity in 21%, and severe in 3% of cases. No fatalities were reported. Withdrawal syndrome was reported in 11 patients (10.3%) and included gastrointestinal symptoms (nausea or vomiting 64%, diarrhea 27%), agitation (36%), tremor (27%), and acute kidney injury (18%). **Conclusion:** The rising number of reports to the Israel Poison Information Center of synthetic cannabinoid use and withdrawal syndrome during the past 5 years suggests increasing use in the population at large. Users had a typical profile (predominantly young males). While most symptoms were mild, considerable morbidity was reported in some cases. Understanding the short- and long-term consequences of synthetic cannabinoid use and law enforcement are ongoing challenges.

## 75. Alcoholic poisonings in adolescents treated in an emergency room in the summer of 2015

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**Objective:** Although the sale and consumption of alcoholic beverages is forbidden to minors (under 18 years of age) in Spain, alcohol is the most prevalent cause of intoxication in adolescents. As in neighboring countries, there is an increasing trend in binge drinking. This phenomenon in our environment is seen primarily in summer, presumably related to tourism. This study examined the incidence and characteristics of acute alcohol intoxication (AAI) in summer in a tertiary care emergency department (ED) serving an area with high density of tourism. **Methods:** An observational retrospective analysis of alcohol intoxication presenting to the ED over three months (1 June to 31 August 2015), analyzing epidemiological data (sex, country of origin and age, time of arrival) and care variables (arrival by ambulance, symptoms, ancillary tests, disposition, length of stay in the ED, documented whether released to adult tutor or guardian and if a legal report was filed). **Results:** In total 42 patients were treated (8.57% of all AAI in the same period), 22 were males (52.4%), 19 were Spanish (45.2%) and 17 were British (40.4%). Most were 17-years-old (69%) with one 13 and one 14-year-old. All patients arrived between 22:00 and 10:00, with the range between 02:00 and 2:59 the most common (21.4%). Most arrived by ambulance (29 cases, 69%). The main symptoms reported were decreased level of consciousness (31, 73.8%), suspected multiple toxins in 7 (16.8%), agitation in 4, other injuries and palpitations in 2, and one patient had head trauma. Quantification of ethanol in blood was performed in 11 cases (26.1%), with an average blood ethanol concentration of 2.01 g/L. In one case, a computerised tomography (CT) scan was performed. The average stay in the ED was 4.29 hours (range 0:56–12:27 hours). All patients were discharged from the ED. There were no deaths or subsequent readmissions, although affiliation data was missing in 5 cases (11.9%). The presence of an adult guardian or tutor was reflected in the discharge report; in nine cases (21.4%), a legal report was filed in 11.9%. **Conclusion:** AAI in minors presenting in summer in the ED accounted for 8.57% of total AAI cases, patients were mainly Spanish and British. Most were seen for decreased level of consciousness with a short average stay and without serious acute complications. Discharge records were poor in reporting to whom the minors were discharged and in filing mandatory legal reports.

## 76. Gamma-butyrolactone overdose with metabolic acidosis treated without dialysis

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**Objective:** Gamma-hydroxybutyrate (GHB) and its prodrug gamma-butyrolactone (GBL) are used as drugs of abuse.[1] A large dose of GBL, rapidly metabolized to GHB, has caused severe metabolic acidosis requiring treatment in an intensive care unit and dialysis in previously published cases.[2,3] We present two cases of GBL poisoning. **Case series:** In separate incidents two 34-year-old patients, a male and a female, were intubated by Emergency Medical Services because of a Glasgow Coma Scale of 3/15. GBL use was suspected on scene in both cases. Both were administered vasoactive drugs (ephedrine, epinephrine and/or norepinephrine) due to hypotension. Their first measured arterial blood gases were pH 6.90, PaCO<sub>2</sub> 6.38 kPa, PaO<sub>2</sub> 15.4 kPa, HCO<sub>3</sub> 9.5 mmol/L, base excess (BE) -23 mmol/L and pH 6.99, PaO<sub>2</sub> 20.5 kPa, PaCO<sub>2</sub> 5.3 kPa, HCO<sub>3</sub> 8 mmol/L, BE -21.3 mmol/L, respectively. In addition to mechanical ventilation and norepinephrine-infusions, they were also administered Ringer's acetate, sodium bicarbonate and fentanyl intravenously. Their acidosis subsided within 10 and six hours, respectively, and neither patient required dialysis. Both recovered without sequelae. The GHB concentrations measured later from blood samples were 1500 and 1400 mg/L, respectively, and were determined by gas chromatography/mass spectrometry according to a previously reported method.[4] Comprehensive toxicological analysis revealed also the following blood drug concentrations: 0.5 mcg/L of fentanyl and 0.37 mg/L of 3,4-methylenedioxyamphetamine (MDMA) in the male patient and alpha-pyrrolidinovalerophenone (alpha-PVP) 0.05 mg/L, amphetamine 0.05 mg/L, ephedrine 0.13 mg/L, fentanyl 0.3 mcg/L, clonazepam 0.22 mg/L, diazepam 0.52 mg/L, nordiazepam 0.17 mg/L, and alprazolam 0.013 mg/L in the female. **Conclusion:** GBL overdose with metabolic acidosis can be successfully treated with supportive care only.

## References

- [1] Schep LJ, Knudsen K, Slaughter RJ, et al. The clinical toxicology of gamma-hydroxybutyrate, gamma-butyrolactone and 1,4-butanediol. *Clin Toxicol (Phila)*. 2012;50:458–470.
- [2] Roberts DM, Smith MW, Gopalakrishnan M, et al. Extreme gamma-butyrolactone overdose with severe metabolic acidosis requiring hemodialysis. *Ann Emerg Med*. 2011;58:83–85.
- [3] Connors NJ, Hoffman RS, Nelson LS. Increased serum osmolality and metabolic acidosis following massive gamma-hydroxybutyrate consumption. *Clin Toxicol (Phila)*. 2013;51:367.
- [4] Elian AA. A novel method for GHB detection in urine and its application in drug-facilitated sexual assaults. *Forensic Sci Int*. 2000;109:183–187.

## 77. All that glitters is not LSD!

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**Objective:** Among the recreational drugs, 2,5-dimethoxy-derived phenethylamines have hallucinogenic properties as lysergic acid diethylamide (LSD). Recently, 2,5-dimethoxy-4-chloroamphetamine (DOC) appeared on the drug market and was responsible for sporadic deaths reported in the literature. We present five clinical cases reported to our Poison Control Centre from March 2014 to March 2015 that could contribute to a better knowledge of this product. **Cases report:** Five men aged 16 to 23 years consumed drugs during a private party (2 cases) or a rave party (3 cases).

**Table 1.** DOC concentrations in patient samples.

Case	Plasma (µg/L)	Urine (µg/L)	Other drugs
1	13	720	MDMA (MDA)
2	10	1300	MDMA (MDA)
3	<10	320	Cocaine, ketamine
4	<10	300	–
5	18	470	Methiopropamine (MPA), pentedrone, alpha-methyltryptamine (AMT)

Four patients said they consumed LSD blotters. The symptoms were primarily psychiatric, all experienced hallucinations (up to 24 hours), were agitated and anxious. Mydriasis ( $n=4$ ) and tachycardia ( $n=2$ , maximum 150 bpm) were also common. One patient experienced seizures. Treatment was supportive. Severity was scored from mild (PSS2, 4 cases) to high (PSS3, 1 case). Toxicological screening was performed by high-performance liquid chromatography with diode-array detection (HPLC-DAD) with quantification by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Results are presented in Table 1. **Conclusion:** DOC, a synthetic amphetamine, is a partial agonist of serotonin receptors. This explains the psychiatric picture dominated by hallucinations. DOC is sold as blotters and falsely named as LSD. Cardiovascular and neurological complications may be severe in young and otherwise healthy individuals. Unfortunately, DOC is not detected by usual amphetamine urine tests. Physicians, toxicologists and analysts should be aware of this novel psychoactive substance consumption trends in order to inform management of patient care and to contribute to a more responsive drug policy.

## 78. Severe clinical toxicity following analytically confirmed use of the synthetic cannabinoid receptor agonist MDMB-CHMICA: a report from the Identification Of Novel psychoActive substance study (IONA)

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**Objective:** Recreational use of synthetic cannabinoid receptors agonists (SCRAs) has become increasingly common in many countries including the UK.[1,2] These substances are often purchased as branded products, which may contain a wide variety of different compounds which often fall outside drug control regulations. Toxicity with SCRAs can be associated with severe adverse events not typically observed with cannabis. This report describes two cases of severe clinical toxicity after use of MDMB-CHMICA (also called MDMB-CHMINACA), an indole-based SCRA, which has recently been found in several branded SCRA products on sale in the UK. **Case reports:** Two males were transferred to hospital on the same day but in separate episodes after smoking a recreational product labelled as “Sweet Leaf Obliteration”. Case 1: A 16-year-old with no significant past medical history, developed severe but short-lived unconsciousness after smoking the product. Use of other drugs was denied. Other clinical findings included

emesis, abdominal pain, tachycardia (maximum 120 bpm), confusion, mydriasis and respiratory acidosis (pH 7.29). Case 2: A 41-year-old chronic cannabis user, collapsed soon after smoking a similar product. Previous exposures to different SCRA products had been uneventful. Physical exam on arrival revealed drowsiness, confusion, hypotension (92/56 mmHg), bradycardia (42 beats/min), hypothermia (34 °C), mydriasis and respiratory acidosis (pH 7.28). Both patients were discharged the day after admission having made a full recovery. MDMB-CHMICA was detected in blood from both patients by liquid chromatography-mass spectrometry (LC/MS) (quantitative measurements are pending). Routine haematology and biochemistry blood tests were unremarkable. **Conclusion:** Analytically confirmed use of MDMB-CHMICA, was associated with reduced level of consciousness, confusion, mydriasis and respiratory acidosis in both patients. Other effects reported with this compound include dizziness, nausea, shortness of breath, chest pain, irregular heartbeat, convulsion and cardiac arrest.[3,4]

## References

- [1] United Nations Office on Drugs and Crime (UNODC) report. Global smart update. March 2015, Vol 13; [cited 2015 Oct 7]. Available at: <https://www.unodc.org/unodc/en/scientists/global-smart-update-2015-vol13.html>
- [2] Trecki J, Gerona RR, Schwartz MD. Synthetic cannabinoid related illnesses and deaths. *N Engl J Med.* 2015;373:103–107.
- [3] WEDINOS working group. Hospitalisation from synthetic cannabinoid MMB-CHMINACA; [cited 2015 Nov 26]. Available at: <http://asfa-carduf.org/wp-content/uploads/2015/07/MMB-CHMINACA-MDMB-CHMICA-alert.pdf>
- [4] Westin AA, Frost J, Brede WR, et al. Sudden cardiac death following use of the synthetic cannabinoid MDMB-CHMICA. *J Anal Toxicol.* 2015;40:86–87.

## 79. Patterns of presentation and clinical toxicity after reported use of methiopropamine: a report from the UK National Poisons Information Service (NPIS)

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**Objective:** Methiopropamine, a thiophene methamphetamine analogue, has recently been sold as a recreational stimulant in the UK [1] and is a common component of several “branded” products, including “Gogaine” and “Synthacaine”. These may also contain other substances (e.g. ethylphenidate, local anaesthetics), although content varies between brands and batches.[2] This study was performed to characterise the pattern of acute toxicity of methiopropamine, as reported by health professionals to the UK’s National Poisons Information Service (NPIS). **Methods:** Review of NPIS telephone enquiries from 1 January 2011 to 27 October 2015 (inclusive). **Results:** NPIS enquiries involving 94 individuals (65 males, 19 females, 10 not recorded, median age

31 years, range 17–64 years) were identified with exposure to methiopropamine or a product previously shown to contain methiopropamine as a major constituent by sample analysis (7 methiopropamine alone; 41 a single methiopropamine-containing product; 46 used more than one substance/branded product). Numbers of cases by year were 15 (2011), 22 (2012), 24 (2013), 19 (2014) and 14 (2015 up to 17 March). Methiopropamine-containing products most commonly involved were “Synthacaine” ( $n = 15$ ), “Gogaine” ( $n = 13$ ) and “Pink Panther” ( $n = 13$ ). Common clinical features reported overall were tachycardia/palpitations (32%), agitation/confusion/anxiety (29%), mydriasis (12%), chest pain (8%), nausea/vomiting (7%), acidosis (6%) and convulsions (6%). There were 4 (4%) cases classified as severe with clinical features including hyperpyrexia, agitation and a reduced level of consciousness requiring ventilation. Methiopropamine exposure was confirmed by analysis of urine in one severe case. **Conclusion:** Interpretation of these data is challenging because of the variable presence of the drug in different branded products, which may also contain other substances. Our results suggest that methiopropamine use predominantly involves younger adults and males and that there were no major changes in presentation rates over the period of study until 2015. Clinical features are consistent with an amphetamine-related substance and with those previously reported in an analytically confirmed case,<sup>[3]</sup> but other co-used substances are likely to make an important contribution.

## References

- [1] Angelov D, O'Brien J, Kavanagh P. The syntheses of 1-(2-thienyl)-2-(methylamino) propane (methiopropamine) and its 3-thienyl isomer for use as reference standards. *Drug Test Anal.* 2013;5:145–149.
- [2] Welsh Emerging Drugs and Identification of Novel Substances Project (WEDINOS); [cited 2015 Nov 2]. Available at: <http://www.wedinos.org/>
- [3] Lee HM, Wood DM, Hudson S, et al. Acute toxicity associated with analytically confirmed recreational use of methiopropamine (1-(thiophen-2-yl)-2-methylaminopropane). *J Med Toxicol.* 2014; 10:299–302.

## 81. An unusual case of cannabinoid hyperemesis syndrome

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**Objective:** A growing number of cases of cannabinoid hyperemesis syndrome (CHS) have been published worldwide. CHS is characterized by repeated vomiting, nausea, flushing and diaphoresis in patients with chronic cannabis use. Hot showers or baths can relieve symptoms. **Case report:** An 18-year-old male presented to the emergency department (ED) with nausea, vomiting, and abdominal pain. In the last two years the patient had been evaluated about ten times in the ED with similar complaints. The year before, he had been admitted to hospital for evaluation but no organic cause was found. Previous investigations, including esophagogastroduodenoscopy and colonoscopy, were normal. On admission he was suffering with hyperemesis, bradycardia and diaphoresis. An electrocardiogram (ECG) showed sinus bradycardia and a chest radiograph was unremarkable. Abdominal ultrasound showed increased parietal colon thickness and free peritoneal liquid. Treatment with intravenous normal saline and high dose metoclopramide was ineffective. Bradycardia was reversed with atropine 0.5 mg IV bolus, but recurred after one hour.

He admitted cannabis consumption a few times in the past. Urinary screening for substances of abuse was positive for tetrahydrocannabinol (THC). After investigations the patient declared that a recent cigarette in reality was tobacco mixed with hashish. All symptoms resolved after 24 hours. To confirm the diagnosis of CHS, the patient admitted that on previous occurrences the hot shower had improved symptoms. **Conclusion:** Cannabinoid hyperemesis is a paradoxical reaction that occurs with long-term cannabis use, resulting in severe nausea, cyclic vomiting, chronic abdominal pain, and compulsive bathing behavior. It often can be missed and confused with various disorders. No clear mechanism has been identified to explain the pathophysiology. One potential mechanism may involve cannabinoid receptor type 1 (CB1) receptors in the gastrointestinal mucosa. Regular cannabis use is considered essential for the diagnosis of CHS. In contrast our patient had an occasional use and passive smoke inhalation. Abstinence from cannabis resolves the symptoms completely. Cannabinoid hyperemesis syndrome can result in repeated visits to the ED and should be considered in younger patients with cannabis use and recurrent nausea, vomiting, and abdominal pain. The timing, location, and characteristics of symptoms can be helpful in determining the diagnosis of CHS, and patients should be asked about the relief of symptoms with hot water bathing. Physicians should be aware of this syndrome.

## 82. Clinical features of paramethoxymethamphetamine (PMMA) poisoning in lethal and non-lethal cases

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**Objective:** Paramethoxymethamphetamine (PMMA), and its metabolite paramethoxyamphetamine (PMA), cause central nervous system stimulation and hallucinogenic effects, like 3,4-methylenedioxymethamphetamine (MDMA). PMMA/PMA poisoning resulting in fatalities has been described.<sup>[1]</sup> We report 5 cases of PMMA/PMA severe intoxication collected in 2 years. **Case series:** Five cases referred to Pavia Poison Control Centre (PPCC) were evaluated (age ranging from 16 to 32 years). Patients did not admit PMMA/PMA consumption: one patient referred to MDMA intake, one to patient amphetamine and cannabis and three patients were unable to report the substance taken. The most common clinical manifestations were severe psychomotor agitation (100%), tachycardia (80%), mydriasis (60%), sweating (60%), hallucinations (40%) and hyperthermia (20%). Immunoenzymatic urinary tests were positive for amphetamine/methamphetamine, MDMA, cocaine and tetrahydrocannabinol (THC). Chromatographic second level laboratory investigations were performed and all patients were positive for PMMA/PMA but also to MDMA ( $n = 4$ ), amphetamine ( $n = 3$ ), THC ( $n = 3$ ), cocaine ( $n = 2$ ), ketamine ( $n = 1$ ) and methoxetamine ( $n = 1$ ). Treatment consisted

of benzodiazepines ( $n=5$ ) and oro-tracheal intubation and respiratory support ( $n=2$ ). Hospital stay ranged from 24 to 96 hours for the patients that needed intensive care treatment. One fatal case was registered; the clinical picture worsened rapidly with metabolic acidosis, hypoglycemia, hyperkalemia, severe hyperthermia, multi-organ failure and severe disseminated intravascular coagulation. Although pharmacological treatments and intensive care support (including depurative techniques) were given, the patient died in 20 hours. The results of blood analysis were: PMMA 615 ng/mL, PMA 91 ng/mL, tramadol 88 ng/mL, MDMA 192 ng/mL, methylenedioxyamphetamine (MDA) < 20 ng/mL, cocaine 28 ng/mL and benzoylcgonine 529 ng/mL. Analysis of a residual part of the tablet taken by the patient revealed PMMA 25 mg and MDMA 11 mg. **Conclusion:** PMMA/PMA intoxication may result in a rapid and fatal outcome. Hyperthermia should be interpreted as a potentially severe risk factor. Nevertheless, the national epidemiological data of abuse of PMMA/PMA cannot be quantified, as the PPCC (with advanced toxicological analysis facilities) and the National Early Warning System detect only patients with acute and severe intoxication. Urine positivity for ecstasy and amphetamines should be considered as cross-positivity to PMMA/PMA (not easily detectable in common laboratories). All the cases were reported to the National Early Warning System. **Acknowledgements:** Study carried out with the support of DPA-Presidency of the Council of Ministers.

## Reference

- [1] Lurie Y, Gopher A, Lavon O, et al. Severe paramethoxymethamphetamine (PMMA) and paramethoxyamphetamine (PMA) outbreak in Israel. *Clin Toxicol (Phila)*. 2012;50:39–43.

## 83. Clinical features of intoxication with 2C-series phenethylamines

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**Objective:** 2C-series phenethylamines intoxication may result in admission to an emergency department (ED). Early diagnosis could ameliorate the clinical management of these patients, but standard urine toxicological screening may detect only a generic positivity to amphetamines or ecstasy. A study was conducted through the national ED network referring to the Pavia Poison Control Centre (PPCC) in order to evaluate the clinical features and prevalence of analytically confirmed 2C-series phenethylamine intoxications in 2014. **Case series:** Among the consecutive cases referred to the PPCC in 2014 for suspected/confirmed poisoning by novel substances of abuse (NPS), intoxications by 2C-series phenethylamines were evaluated ( $n=10$ ). Cases were assessed for age, history, acute clinical manifestations, outcome, treatment and toxicological-analytical investigations. Among 10 cases of 2C-series phenethylamine intoxication, 8 involved 2-Cl and 2 the 2-CE series. Patients did not admit to use of 2C-series drugs; 3 patients were unable to report the substance(s) taken,

and 7 admitted to use of another NPS. The most common clinical manifestations were severe psychomotor agitation (60%), tachycardia (50%), hallucinations (30%), mydriasis (30%), gastrointestinal discomfort, drowsiness, confusion, coma, seizures and hyperthermia (20% each); no lethal cases were registered. Second level laboratory investigations were performed in all the cases (non-urgent analysis). All urine samples were positive for 2C-series drugs but also for tetrahydrocannabinol (THC) ( $n=8$ ), 3,4-methylenedioxyamphetamine (MDMA) ( $n=4$ ), amphetamines ( $n=3$ ) and ketamine ( $n=1$ ). The treatment consisted of benzodiazepines ( $n=10$ ), intubation and respiratory support ( $n=4$ ). Hospital stay ranged from 10 to 96 hours for the patients that needed intensive care treatment. **Conclusion:** The use of 2C-series phenethylamines cannot be quantified in Italy, as the PPCC (with advanced toxicological analysis facilities) and the National Early Warning System detect only patients with acute and severe intoxication. Urine positivity for ecstasy and amphetamines can be associated with 2-C series phenethylamines intoxication (not easily detectable in common laboratories). All the cases described here were reported to the National Early Warning System. **Acknowledgements:** Study carried out with the support of DPA - Presidency of the Council of Ministers.

## 84. Accidental intoxication with cannabis after mistaking it for frozen food

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**Objective:** In France, cannabis is the most commonly used illicit drug among the general population, mainly by smoking. It can also be ingested, especially as pastries (e.g. space cake, etc). Accidental ingestion occurs more often in young children who eat cannabis left within their reach, however, a few cases of accidental ingestion of cannabis have been reported in adults after mistaking it for food or being unaware the food was made with cannabis. We describe two outbreaks of cannabis exposure involving three patients in 2014 and one in 2015. This occurred in unusual but similar circumstances: a mix up with food stored in the freezer. **Case series:** The first three patients shared the same dishes while the other one ate alone. All four patients experienced vomiting and neurological symptoms within one hour following ingestion. The clinical presentation, poorly suggestive of typical food poisoning, was characterized by acute alteration of consciousness, dizziness, ataxia, nausea and vomiting. The anamnesis and the circumstances of occurrence were secondarily clarified. The first three patients ingested pasta seasoned with a sauce found in the freezer, which turned out to be marijuana butter, unlabelled and prepared by a third party. The other patient accidentally ate frozen cannabis leaves which had been mistaken for frozen spinach. All four patients tested positive for cannabis on urine toxicology screen. They all recovered within 36 hours following ingestion. **Conclusion:** Accidental cannabis poisoning in adults can occur in unusual circumstances, through ingestion of unlabelled material mistaken for frozen food, facilitated by the storage place. An alleged food poisoning with neurological symptoms such as psychomotor impairment, drowsiness and dizziness may suggest food confusion with marijuana. A routine urine screening test for 11-nor-9-carboxy- $\Delta^9$ -tetrahydrocannabinol (THCCOOH) can help to confirm the diagnosis.

## 85. Futile fight – trends in poisoning with drugs of abuse in Hungary

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**Objective:** To determine trends and specific features in the clinical course and epidemiology of acute poisonings of different types of novel psychoactive substances (NPS). **Methods:** Retrospective evaluation of clinical records of patients admitted to our department between 1 December 2013 and 30 November 2014. We processed the data of the patients who were admitted to our department after consumption of any drug, who showed symptoms related to their drug taking and had no other cause of their symptoms. **Results:** There were 2036 cases of acute poisoning with NPS involving 1611 patients (1459 patients had one episode and 154 had >1). Length of hospital stay was <6 hours in 170 patients, 6 to 24 hours in 1262 patients and >24 hours in 604 patients. There were a total of 359 acute poisonings caused by classic drugs of abuse and 1677 acute poisonings caused by NPS. Three new designer drugs have become widespread (causing 1642 intoxications): "penta crystal" (typically containing pentadrone) in 527 patients, "music" (typically containing alpha-pyrrolidinovalerophenone [alpha-PVP] or PV8) in 362 patients and "bio-grass" or "herbal smoke" (containing various synthetic cannabinoids and often cathinones) in 753 patients. There were 1216 males and 461 females intoxicated by NPS; mean age was 25.2 years, but in the autumn a third of patients (132/439) were younger than 18 with regard to the use of herbal smoke. The use of classic amphetamine-like stimulants resulted in increased psychomotor activity (82.3%), increased heart rate (76.6%) and blood pressure (71.2%), dilated pupils (70.8%) and chest complaints (28.1%). With cathinones the most characteristic symptoms were agitation (78.9%), confusion (72.1%), hallucinations (45.4%), paranoid psychosis (42.5%), aggression (34.7%) and trauma (27.6%). Cannabis typically caused dizziness (86.9%), nausea/vomiting (80.6%) and mild hypotension (29.1%). After using herbal smoke central nervous system depression (55.3%), confusion (53.25%) and hallucinations (24.3%) occurred frequently. According to the Poison Severity Score intoxication caused by the classic stimulants was predominantly mild (40.6%) or moderate (51.1%); however, the new cathinone-type drugs typically caused moderate (48.1%) and severe (34.9%) poisoning. We identified a great number of moderate (55%) or severe (13.8%) intoxications due to the use of "bio-grass". The symptoms caused by the use of synthetic cannabinoids changed season by season. There were 3 fatal cases. **Conclusion:** The recreational drug market has changed profoundly, including type of substances available and their consequences. NPS more often result in serious psychosis, aggressive state and traumatic injuries than classic drugs of abuse.

## 86. A synthetic cannabinoid receptor agonist (AB-FUBINACA)-associated fatality

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**Objective:** Synthetic cannabinoid receptor agonists (SCRAs) are currently popular novel drugs of abuse.[1] Increased use of SCRAs has occurred despite their ban by the US Drug Enforcement Agency and some local jurisdictions. Few confirmed SCRA-associated deaths are reported.[2,3] In 2015, the number of SCRA-related emergency department (ED) visits in our area skyrocketed. Despite increased use, this is the first confirmed SCRA-associated fatality in our area. **Case report:** A 35-year-old man with a history of polysubstance abuse was reported to have agitated behavior after suspected cocaine and "K2" (SCRA) use. Upon arrival, he was severely agitated but verbal with equal and reactive pupils. Due to persistent agitation, he was physically restrained and given 10 mg of intramuscular midazolam. A computerised tomography (CT) scan of the brain was unremarkable and a chest radiograph suggested aspiration pneumonia. The patient was endotracheally intubated and subsequently developed a pulseless electrical activity (PEA) arrest. Resuscitative measures were unsuccessful and he was pronounced dead. On autopsy, the medical examiner noted insignificant minor traumatic injuries that were consistent with combative behavior and physical restraints and did not contribute to death. He was noted to have cardiac hypertrophy with concentric left ventricular hypertrophy and abundant white frothy material in the bronchi without other structural abnormalities. Toxicology testing identified the presence of AB-FUBINACA, cocaine, and benzoylecgonine. In femoral blood, the AB-FUBINACA concentration was >2.0 ng/mL, benzoylecgonine concentration <0.05 mg/L and cocaine was not detected suggesting that cocaine use was more remote. Cocaine and benzoylecgonine were detected in the urine. Urine was not tested for SCRAs. In vitreous humour, the cocaine concentration was <0.05 mg/L and benzoylecgonine was 0.08 mg/L; SCRA was not tested. The cause of death was determined to be "acute mixed drug intoxication (cocaine and synthetic cannabinoid receptor agonist (AB-FUBINACA))." **Conclusion:** During the surge of reported SCRA use in our area, this is a single confirmed SCRA-(AB-FUBINACA)-associated fatality.

### References

- [1] Su MK, Seely KA, Moran JH, et al. Metabolism of classical cannabinoids and the synthetic cannabinoid JWH-018. *Clin Pharmacol Ther.* 2015;97:562–564.
- [2] Trecki J, Gerona RR, Schwartz MD. Synthetic cannabinoid-related illnesses and deaths. *N Engl J Med.* 2015;373:103–107.
- [3] Shanks KG, Winston D, Heidingsfelder J, et al. Case reports of synthetic cannabinoid XLR-11 associated fatalities. *Forensic Sci Int.* 2015;252:e6–e9.

## 87. Cases of suspected drink spiking presenting to a Danish emergency department

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**Objective:** The number of presentations to emergency departments in Denmark due to suspicion of forced drug exposure by drink spiking is unknown. This study describes the number and pattern of presentations on suspicion of ingestion of a spiked drink to a Danish emergency department (ED).

**Methods:** We reviewed medical records from presentation to the ED at the Bispebjerg Hospital, Copenhagen, between 10 January 2013 and 30 September 2014, to identify patients who had ingested a spiked drink. We extracted clinical and anamnestic data and rated patients' clinical condition retrospectively using the Poison Severity Score (PSS). **Results:** Twenty-three out of 571 referrals with suspected intoxicants or drug intoxication over the study period were suspected victims of drink spiking. This corresponds to 0.27 out of 1000 presentations to the emergency ward. The mean age was 22 years (range 15–35 years). Nineteen were women. All presented to the emergency ward within 8 hours of suspected exposure, 16 within 4 hours and 5 within 2 hours. Five patients were admitted by ambulance, while the rest presented themselves. Four patients suspected 3,4-methylenedioxymethamphetamine (MDMA) as the possible substance and one suspected gammahydroxybutyrate (GHB). In seven cases, the staff suspected ethanol to be the only exposure; however, serum ethanol was only measured in six cases (mean 1.4, range 0.9–2.0). Five patients were screened for paracetamol and acetylsalicylate poisoning (all negative). No further toxicological screening in biospecimens was done, although routinely collected in all cases. Five patients reported rapidly developing severe cerebral symptoms or black out. Seven patients showed no symptoms at presentation (PSS=0), six had signs of mild intoxication (PSS=1), eight showed symptoms of severe acute poisoning (PSS=2) and two patients had life-threatening symptoms (PSS=3). All survived. **Conclusion:** The clinical picture of patients presenting to the ED due to possible exposure to a spiked drink ranged from asymptomatic to severe intoxication. Incomplete information, concomitant alcohol consumption, a wide range of possible exposures and random use of toxicological screening, impede uniform clinical management. Stays at the ED were usually short and without follow up care.

## 88. Trend analysis of novel psychoactive substances (NPS) detected in pooled urine samples from street urinals in London, UK over 18 months

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**Objective:** Current methods for determining use of recreational drugs including novel psychoactive drugs (NPS) rely on population/subpopulation self-reported surveys. The reliability of these may vary due to the inaccuracies of self-reported use and/or variation of drug content. Therefore analysis of biological samples can be helpful in confirming the drugs actually used. This study aimed to determine changes in patterns of NPS detected in street urinals in London over an 18 month period. **Methods:** Anonymised pooled urine samples were collected using 12 stand-alone four-person urinals in the same geographical locations in central London, UK on the first Saturday night each month from July 2013 to December 2014. Samples were analysed using

full-scan accurate mass high-resolution liquid chromatography tandem mass-spectrometry against databases containing more than 1700 drug compounds and their metabolites. Data were analysed and we report the number of months the NPS was detected, the range of urinals positive per month and the percentage detection rate (PDR: urinals positive for the NPS as a percentage of the total urinals screened in the months the NPS was detected). **Results:** In total 18 NPS were detected with a median (IQR) of 5 (4–5.5) NPS detected per month. Four NPS were detected consistently over the 18 months: mephedrone was detected every month (2–9 urinals/month, PDR 52%); methiopropamine in 16 months (1–4 urinals/month, PDR 16%); methylhexanamine in 14 months (1–4 urinals/month, PDR 19%); and methylone in 11 months (1–8 urinals/month, PDR 30%). The remaining 14 NPS were detected in 6 or fewer months: ethylone in 6 months (range 1–4 urinals/month, PDR 24%); N,alpha-diethylphenethylamine in 4 months (range 1–3 urinals/month, PDR 15%); ethylamphetamine in 2 months (8 urinals in one month, 10 urinals the other [PDR 75%]); 1-(3-chlorophenyl)piperazine and 5F-AKB-48 both detected in 2 months (1 urinal/month, PDR 8%); AKB48 detected in 1 month in 5 urinals (PDR 42%); and 1,4-trifluoromethylpiperazine, N-ethylphentermine, 1-(benzofuran-5-yl)-N-ethylpropan-2-amine, 1-benzylpiperazine, ethylphenidate, methylphenidate, phenylisobutylamine and 5F-APICA/STS-135 each detected in one urinal in one month only (PDR 8%). **Conclusion:** NPS were commonly detected in this study, in particular mephedrone which was seen throughout the whole of the study. There was variation in many other NPS with short-term detection of some across the 18 months. Analysis of anonymised pool urine samples from portable urinals can be used to monitor trends in NPS use over time and be triangulated with other indicators to build a fuller picture of the prevalence of NPS use.

## 89. Adverse events associated with tianeptine use and abuse

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**Objective:** To describe two cases of adverse events occurring from tianeptine use. Tianeptine is an atypical antidepressant with abuse potential [1] that is unregulated and available for purchase without a prescription in the US. **Case report:** Case 1: A 23-year-old male medical student presented to the emergency department (ED) for altered mental status and reported several episodes of "blacking out" recently. He admitted to using tianeptine purchased on the Internet without a prescription to treat anxiety for the past 3 months. His vitals were temperature 36.9°C, heart rate 86/min, blood pressure 130/79 mmHg, respiratory rate 16 and oxygen saturation 100%. On physical exam he was alert but appeared anxious and easily agitated. His pupils were 6 mm bilaterally and reactive, with dry mucus membranes, and hypoactive bowel sounds. His electrocardiogram (ECG) had normal QRS and QTc intervals. His laboratory findings were unremarkable and the patient was observed in the ED for 8 hours before being seen by psychiatry and discharged home. Case 2: A 27 year-old-male laboratory researcher presented to the ED unresponsive after abusing tianeptine and alcohol. His vital signs were temperature 37°C, heart rate 78/min, blood pressure 129/63 mmHg and oxygen saturation 47% with infrequent shallow respirations. He was cyanotic, with pinpoint pupils and horizontal nystagmus. He was

administered 0.4 mg naloxone IV, with dramatic improvement in mental status and increase in respiratory rate. His ECG was normal sinus rhythm of 85/min, with QTc of 442 msec and QRS duration of 102 msec. The serum ethanol concentration was 238 mg/dL (51.67 mmol/L). Urine drug screen was negative for opiates. He was administered another 0.4 mg naloxone IV for recurrent respiratory depression, and admitted to the medical intensive care unit (MICU) on a naloxone drip. **Conclusion:** We describe two cases of patients experiencing adverse effects from tianeptine purchased over the Internet. Tianeptine is structurally similar to tricyclic antidepressants, and was recently described as having mu opioid receptor agonism.[2] Tianeptine is available without prescription in the US, has high abuse potential, and can cause respiratory depression. Reversal of tianeptine-related respiratory depression with naloxone is not well-documented prior to these case reports.

## References

- [1] Gassaway MM, Rives ML, Kruegel AC, et al. The atypical antidepressant and neurorestorative agent tianeptine is a mu-opioid receptor agonist. *Transl Psychiatry*. 2014; 4:e411.
- [2] Vadachkoria D, Gabunia L, Gambashidze K, et al. Addictive potential of tianeptine – the threatening reality. *Georgian Med News*. 2009;174:92–94.

## 91. A review of enquiries received by the UK National Poisons Information Service (NPIS) from England and Wales involving calcium channel blocking drugs 2009–2013

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**Objective:** To report the incidence of enquiries to the NPIS concerning calcium channel blocking (CCB) drugs in England and Wales. **Methods:** Records of telephone enquiries received from England and Wales by the NPIS between 1 January 2009 and 31 December 2013 were reviewed. Enquiries involving calcium channel blocking (CCB) drugs were examined and those from hospitals were analysed further for details regarding admission to the intensive care unit (ICU), features, treatment modalities and outcome. **Results:** The NPIS received 226,940 telephone enquiries during this period. Of these 2865 (1%) related to CCB drugs, alone or in combination with other medications. There was no significant change in rate over time. Except for a small peak of accidental ingestions by children under 5 years, enquiries regarding CCBs increased with age. Patients over 70 years accounted for 42% of enquiries. Amlodipine was most commonly taken (52% of CCBs) (diltiazem 20%, nifedipine 9%, felodipine 8%, verapamil 6%, lercanidipine 4%, and lacidipine 1%). There were 510 enquiries (concerning 427 patients) from hospitals regarding symptomatic cases. Of these, 185 were admitted to ICU. The majority of exposures were intentional ( $n = 358$ ); 24 were accidental, 23 due to therapeutic error and 22 due to other circumstances. CCBs taken alone accounted for 65 cases. In two cases it was unclear if other drugs were taken, while 360 cases involved multiple drugs. Symptoms documented at time of enquiry or follow up included hypotension (275 cases), bradycardia (125), acidosis (125), central nervous system (CNS) depression (168), other CNS features (158); abnormal

renal function (68) and pulmonary oedema (6). Treatments used included IV fluids (297 cases), calcium gluconate or chloride (165), ionotropes (127), glucagon (112), insulin dextrose infusion (87) and Intralipid (37). Of the 29 deaths reported (17 male, 12 female), 25 were intentional overdoses. Five related to CCBs taken alone, all of which involved verapamil. Other deaths involved amlodipine (15), diltiazem (3), nifedipine (2), lercanidipine (1) and nimodipine (1). **Conclusion:** CCB drugs account for a small proportion of deaths reported in cases discussed with the NPIS, and commonly involve multiple drug overdose. Amlodipine is the most frequent agent reported but a much higher proportion of verapamil enquiries result in death and accounted for all the deaths where only one agent was taken. This may reflect inherent differences in toxicity, but may also reflect different demographics and underlying medical conditions. Linking these findings to prescribing and demographic data would allow consideration of relative toxicity.

## 92. Central nervous system toxicity following mefenamic acid overdose: an analysis of UK National Poisons Information Service Data

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**Objective:** Mefenamic acid overdose has been linked with a greater risk of central nervous system (CNS) toxicity, especially convulsions, than other non-steroidal anti-inflammatory drugs (NSAIDs).[1] This is of concern because mefenamic acid has been prescribed mainly for menstrual symptoms,[2] although recent evidence does not demonstrate efficacy or safety advantages over other NSAIDs [3,4] and also because of the relatively high risk of self-harm, including drug overdose, in young females.[5] We compare the CNS toxicity profile of mefenamic acid following overdose with that of ibuprofen, diclofenac and naproxen, using data collected routinely by poisons centres in the UK. **Methods:** National Poisons Information Service (NPIS) telephone enquiries related to mefenamic acid, ibuprofen, diclofenac and naproxen were analysed for the 7 year period January 2007 to December 2013. **Results:** There were 22,937 NPIS patient-specific telephone enquiries related to the NSAIDs studied, including mefenamic acid (925), ibuprofen (17,302), diclofenac (3385) and naproxen (1325). Patients taking mefenamic acid were younger and more commonly female. CNS toxicity was reported more frequently following overdose with mefenamic acid than the other NSAIDs (OR 7.77, 95% CI 5.68 to 10.62,  $p < 0.001$ ). Convulsions were substantially more common after overdose with mefenamic acid than with the other NSAIDs combined (OR 81.5, 95% CI 27.8 to 238.8,  $p < 0.001$ ). Ingested dose and age (highest risk in 20–30 year age group) were significant predictors of CNS toxicity ( $p < 0.001$  and  $< 0.05$ , respectively), but not sex. **Conclusion:** Overdose with mefenamic acid is associated with a significantly increased risk of



neurological toxicity, especially convulsions, compared with other NSAIDs. As mefenamic acid has no therapeutic superiority over other NSAIDs, and because of the increased risk of self-harm in teenagers and young adults, to whom the drug is most commonly prescribed, it should only be prescribed when safer alternatives are contraindicated or not tolerated.

## References

- [1] Balali-Mood M, Proudfoot A, Critchley J, et al. Mefenamic acid overdose. *Lancet*. 1981;1:1354–1356.
- [2] Baum C, Kennedy D, Forbes M. Utilization of nonsteroidal anti-inflammatory drugs. *Arthritis Rheum*. 1985;28:686–692.
- [3] Marjoribanks J, Proctor M, Farquhar C, et al. Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. *Cochrane Database Syst Rev*. 2010;CD001751.
- [4] Lethaby A, Duckitt K, Farquhar C. Non-steroidal anti-inflammatory drugs for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2013;CD000400.
- [5] Hawton K, Saunders K, O'Connor R. Self-harm and suicide in adolescents. *Lancet* 2012;379:2373–2382.

## 93. Improving the management of a poisoned patient: how complete is the initial information provided by emergency physicians to poisons centers?

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**Objective:** One of the missions of Poison Control Centers (PCC) is to be consulted on the “diagnosis, prognosis and treatment of poisonings”. [1] Enquiries are frequently received from emergency physicians. [2] As with any call center, the toxicologist needs to provide a prompt and appropriate response and in order to achieve this the information received needs to be as accurate as possible. The objective of this study was to evaluate the relevance of the information that emergency physicians are able to give when they call the PCC for the first time and to determine if the information provided makes it possible to propose an appropriate response for the best management of the patient. **Methods:** A prospective study was conducted between 1 January and 31 August 2015 analyzing the first call received by the territorial PCC from an emergency physician for a poisoned patient. On receipt of an enquiry the toxicologist completes a specific questionnaire recording all the information the emergency physician provides without reference to the patient’s record including the nature of the toxin, the (ingested) dose, the time, the route and the duration of exposure, the age, the weight, the medical history of the patient, the clinical signs, the electrocardiogram (ECG), the suicidal or accidental nature, and any prior decontamination. The primary endpoint was the rate of questionnaires completed. **Results:** In total 300 calls were included. Of these only 7% were completed to the maximum and 59% gave at least 80% of the expected information. Body weight and ECG (if deemed appropriate) were missing in 50% of cases. The nature of the toxin was missing in 28% of cases and 8% did not have information on the dose. Information on prior decontamination was lacking in a third of cases. The information collected was not influenced by the

institution where the enquiry originated from. **Conclusion:** Some essential information is often lacking on the first call. Emergency physicians need to be better informed about the information they need to provide to the toxicologist when they call the PCC. This will facilitate a more complete and specific answer and save time for both emergency physicians and toxicologists.

## References

- [1] Mowry JB, Spyker DA, Cantilena LR, et al. 2013 Annual Report of the American Association of Poison Control Centers’ National Poison Data System (NPDS): 31st Annual Report. *Clin Toxicol (Phila)*. 2014;52:1032–1283.
- [2] Labadie M, Penouil F, Capaldo L. Rapport d’Activité et de Toxicovigilance. Centre antipoison et de toxicovigilance d’Aquitaine et de Poitou-Charentes; 2014.

## 94. Poisoning by carbon monoxide in Morocco: 1991–2013

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**Objective:** The goal of this study is to describe the details related to patient statements, and to evaluate the spatiotemporal evolution of carbon monoxide poisoning reported by all regional health directorates to the Centre Anti Poison et de Pharmacovigilance du Maroc (CAPM). **Methods:** A retrospective study of all cases of carbon monoxide reported to the CAPM during the period 1991 to 2013. The CAPM has a database of cases derived from two sources: Intoxication declaration forms of poisoning cases received from health delegations throughout the kingdom and toxicological forms completed by doctors during calls received by the center from the public and health professionals working in public facilities. In all cases, the CAPM physician makes a risk assessment and follows the information to completion by regular telephone contacts until the final evolution of patient. The data collected includes the variables: date, time of poisoning, the person who reported the case, origin, patient (sex, age, weight, pregnancy), toxin/substance suspected, intoxication (isolated or collective circumstances, place, route, symptoms, treatment and evolution). Age groups adopted were those of the International Programme on Chemical Safety (IPCS) of the World Health Organization (WHO). The assessment of the poisoning severity was made using the Poisoning Severity Score (PSS). The descriptive analysis focused on the demographic characteristics and the clinical signs and evolution of carbon monoxide poisoning in Morocco. Data analysis was performed in EpiInfo software and Excel. **Results:** Between 1991 and 2013, there were 25,363 cases involving carbon monoxide poisoning reported to the CAPM. The average age of patients was 26.1 ± 15.8 years and the male:female sex ratio was 0.48. Poisoning was accidental in 99.2% of cases, mostly in private residences (96.8%) and during winter. Most cases (89.31%) occurred in urban areas. The region of Meknès-Tafilalet, in north-central Morocco, was the most affected with 17.3% of cases. The most common symptoms reported were central and peripheral nervous system disorders (38.8%), gastrointestinal disorders (35.9%) and respiratory signs (21.7%). Death occurred in 1.1% of cases. **Conclusion:** This qualitative and quantitative study allows us to highlight the dangers and risks of carbon monoxide poisoning. Also, it provides us with the opportunity to plan a strategy against the harmful effects of carbon monoxide poisoning in Morocco.

## Reference

- [1] Aghandous R, Chaoui H, Rhalem N, et al. Poisoning by carbon monoxide in Morocco from 1991 to 2008. *J Pak Med Assoc.* 2012;62:335–338.

## 95. Toxicovigilance of poisoning cases in the Meknes Tafilalet region, Morocco during 2013–2014

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**Objective:** In Morocco, toxicovigilance is a public health surveillance system which sometimes requires supplemental data from specific studies targeting a region or a product group in order to develop a more representative epidemiologic profile. This study aimed to collect poisoning cases directly from hospital records. **Methods:** The Meknes Tafilalet (MT) region of Morocco includes 6 cities: the prefecture of Meknes, being the administrative center of the region, and 5 other provinces (El Hajeb, Ifrane, Khénifra, Errachidia and Midelt). We conducted a retrospective, cross-sectional study on poisoning cases admitted to emergency medical facilities in the region from 2013 to 2014. All patients with poisoning were included. All the data was analysed using Epi Info software as well as MS Excel (statistical tool and cross tables). **Results:** There were 2810 poisoning cases in the Meknes Tafilalet region over the 2-year period. The highest number of poisoning cases occurred in December. The occurrence of poisoning cases was more important in urban areas; the highest number of poisoning cases occurred in Meknes, followed by Ifrane. The sex ratio (M/F) was 0.64. The mean age of poisoned patients was  $26.7 \pm 16$  years. Over half the cases (52.5%) were attributed to gases. The exposure was non-intentional in 90.3% of cases and the majority of cases occurred at home (89.9%), followed by exposures in public areas (8.5%). Symptoms occurred in 29% of cases. The admission grade was level 2 in 96.2% of the cases and 1.3% of cases were fatal. **Conclusion:** The toxicovigilance system, elaborated by the Centre Anti Poison et de Pharmacovigilance du Maroc (CAPM), provides information on poisoning cases and enables the construction of an epidemiological profile on poisoning and follow up within a spatio-temporal framework in Morocco.[1] In order to improve the system's quality and performance, the commitment and willingness of the people involved are essential, with coordination at the national level, rationalization of information inside/between regions with the CAPM and institutionalization of its activities are essential.

## Reference

- [1] Rhalem N, Chaoui H, Semlali I, et al. Exhaustivité des données de toxicovigilance au Maroc. Implication des services de santé publique et de surveillance épidémiologique. *Toxicologie Maroc.* 2012;15:8–15.

## 96. Paediatric battery ingestion: the experience of the UK National Poisons Information Service (NPIS)

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**Objective:** Button battery ingestion by children has recently been the subject of a patient safety alert issued by National Health Service (NHS) England. The alert was issued to raise awareness of the risk of death and serious harm from delays in recognising and treating ingestion of button batteries.[1] This study was performed to characterise the patterns of toxicity associated with ingestion of batteries (regardless of type) by children reported to the UK National Poisons Information Service (NPIS) and the characteristics of those involved. **Methods:** The NPIS national telephone enquiry database (UKPID) was interrogated for enquiries involving ingestion of any type of battery by a child (0–12 years) for a 6-year period (2009–2014). **Results:** Of 650 enquiries (603 unique cases) identified, 499 (82.7%) involved patients reported to be asymptomatic at the time of presentation. The most common features reported were abdominal pain (3.7%), vomiting (1.5%), melaena (1.3%) and diarrhoea (1.1%). Cases were reported to the NPIS with a median of 1.5 hours post-ingestion, with 31% reported within 0.5 hours. Ingestion of batteries occurred most often within the 1–3 year age group (58%) and was more common in boys (60.3%). The majority of exposures occurred at home (98.6%). The maximum WHO/IPCS/EC/EAPCCT Poisoning Severity Score (PSS) [2] was available for 510 (78.4%) enquiries and was recorded as 0 (no effect, 76%), 1 (mild effects, 19.8%), 2 (moderate, 1.7%) or 3 (severe, 0.59%). When results of imaging were available (79 enquiries) batteries were most commonly found to be in the stomach (61.3%) or at/past the pylorus (12.7%). In 3 cases (3.8%) the battery was located in the oesophagus. **Conclusion:** Paediatric battery ingestion can occasionally result in severe toxicity, but this experience suggests most cases are asymptomatic at first point of contact with a healthcare professional. Lodging of batteries in the oesophagus, which may cause severe local necrosis, is not common, although information on battery location is often unavailable at the time of enquiry. Further and more complete follow up of NPIS enquiries is needed to evaluate long-term sequelae.

## References

- [1] NHS England. Patient safety alert – risk of death and serious harm from delays in recognising and treating ingestion of button batteries (NHS/PSA/W/2014/0172014); [cited 2015 Oct 15]. Available at: <https://www.england.nhs.uk/2014/12/19/psa-button-batteries/>
- [2] Persson HE, Sjöberg GK, Haines JA, et al. Poisoning Severity Score: Grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998;36:205–213.

## 97. Quality assessment of alkalinization recommendation by Poison Center personnel

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**Objective:** Quality management is an essential component of poison center accreditation. This includes ongoing collection, monitoring, analyzing data, and taking action where indicated to improve quality. As a component of quality improvement, periodic review of the recommendations of specialists in poison center information (SPIs) should be performed. The recommendation for the administration of alkalinization by a SPI may occur for a variety of reasons, some which may require on-call clinical toxicologist consultation. This quality assurance study was performed to determine if alkalinization was recommended for an approved indication and whether the SPI appropriately called clinical toxicologist back-up. **Methods:** We identified all human exposure cases from a single poison center database where alkalinization was charted as performed and/or recommended between 1 January 2015 and 30 June 2015. Through a detailed chart review of both fields and notes, we assessed demographic characteristics (age, gender, hospital location), select clinical effects (e.g. conduction disturbance, QRS prolongation, dysrhythmia, asystole, cardiac arrest, acidosis, anion gap increase, hypotension, rhabdomyolysis), and medical outcome. Charts were further reviewed to assess whether the on-call clinical toxicologist was consulted as part of the management of the patient. **Results:** Of the 130 cases where alkalinization was recommended and/or performed, the cases were predominantly adults over 18 years (91.5%) and females (56.2%). Clinical effects indicated through chart review included the following: conduction disturbance excluding QRS prolongation (8.5%), QRS prolongation (39.2%), dysrhythmia (6.2%), asystole (3.8%), cardiac arrest (5.4%), acidosis (55.4%), anion gap increase (36.9%), hypotension (36.9%), and rhabdomyolysis (9.2%). The clinical toxicologist was consulted in the majority of cases ( $n=94$ ; 72.3%). Polysubstance exposures were reported among half of cases, and substances most commonly reported included aspirin ( $n=36$ ; 27.7%), ethanol ( $n=21$ ; 16.2%), and unknown drugs ( $n=18$ ; 13.8%). Approximately 90% of patients had moderate or greater clinical effects, and 8 patients (6.2%) died. Alkalinization was recommended by SPIs in 53.8% of cases whereas in 46.2% of cases it had already been performed prior to SPI involvement. Of those cases where the SPI recommended alkalinization, 52.8% were deemed appropriate and 72.9% appropriately called back-up. **Conclusion:** Quality assessment is an integral component of poison center management and accreditation. SPI alkalinization recommendations should be reviewed periodically. Future studies to evaluate internal versus external practices regarding alkalinization are warranted.

## 98. Factors predicting axonal degeneration of the optic nerve after methanol-induced acute optic neuropathy

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**Objective:** The mechanism by which methanol causes toxicity to the visual system is not well understood. We examined patients with acute methanol poisoning to determine the character of optic nerve axonal degeneration. **Methods:** A prospective cross-sectional study was conducted. Measurement of full-field visual evoked potential with monocular checkerboard pattern-reversal stimulation was performed 3–8 and 24–28 months after discharge in patients with acute methanol poisoning. The amplitudes of N1P1 and P1N2 components of the evoked response were used for analysis of axonal loss. **Results:** In total 54 patients (mean age  $46.7 \pm 3.7$  years) were studied. Of these 13 of 50 patients (26%) had abnormal amplitudes at the first examination (including the patients with nonrecordable amplitudes) and 37 patients had normal amplitudes. Mean N1P1/P1N2 amplitudes for right eyes (REs) were  $6.30 \pm 1.10/8.70 \pm 1.50$   $\mu\text{V}$  and for left eyes (LEs) were  $6.56 \pm 1.00/8.30 \pm 1.40$   $\mu\text{V}$ . The group with abnormal amplitudes had lower arterial pH ( $p=0.009$ ), bicarbonate ( $p=0.036$ ), higher base deficit ( $p=0.005$ ), glucose ( $p=0.015$ ), and lactate ( $p=0.018$ ). At the second examination (45 patients with initial examination and 4 additional patients), insignificant amplitude changes were registered (REs  $6.50 \pm 1.10/9.80 \pm 1.60$   $\mu\text{V}$ , LEs  $6.40 \pm 1.10/9.30 \pm 1.60$   $\mu\text{V}$ ; both  $p > 0.05$ ). In 2 of 44 REs (5%) and in 4 of 45 LEs (9%) with 2 consecutive examinations the initially normal amplitudes deteriorated to abnormal values. In 3 of 45 patients (7%) the abnormal amplitudes deteriorated in both eyes indicating ongoing chronic neuronal degeneration. The dynamics of amplitude deterioration correlated with serum lactate ( $r=0.533$ ;  $p<0.001$ ), glucose ( $r=0.462$ ;  $p=0.005$ ) and formic acid ( $r=0.380$ ;  $p=0.046$ ) concentrations on hospital admission. There was also correlation between the magnetic resonance signs of hemorrhagic brain lesions and the amplitude changes ( $r=-0.535$ ;  $p<0.001$ ). **Conclusion:** The main finding was the functional evidence of neuronal loss in 26% of the patients 3–8 months after acute methanol-induced optic neuropathy. The process of chronic optic nerve axonal degeneration and neuronal loss can continue for at least 2 years in severely poisoned patients. No significant changes in amplitude of evoked complexes were observed during the 2-year period in most patients with initial normal measurements. No patients with initial abnormal amplitudes recovered to normal values 2 years after discharge.

## 99. Optic nerve remyelination after acute methanol neuropathy: a 2-year prospective study in 54 patients

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**Objective:** Knowledge of biochemical predictors associated with the dynamics of remyelination of the optic nerve and objective measures of this process are critical in both the prediction of the character of long-term visual sequelae of acute methanol poisoning and in the assessment of the clinical effectiveness of therapeutic interventions. We studied patients with acute poisoning to

determine the prevalence and dynamics of optic nerve remyelination after methanol-induced optic neuropathy. **Methods:** A prospective study in patients with acute methanol poisoning. Measurement of full-field visual evoked potential with monocular checkerboard pattern-reversal stimulation was performed 3–8 and 24–28 months after discharge from hospital. The latency of the positive peak (P1) was used for the analysis of remyelination dynamics. **Results:** In total 54 patients (mean age  $46.7 \pm 3.7$  years) were studied. Of these, 27 patients had abnormal P1 latencies. Mean P1 latency for right eyes (REs) was  $115.3 \pm 2.1$  ms and for left eyes (LEs) was  $117.4 \pm 3.2$  ms. The group with abnormal latency had lower arterial pH ( $p=0.017$ ), higher anion gap ( $p=0.013$ ), methanol concentration ( $p=0.027$ ), base deficit ( $p=0.033$ ) and lactate ( $p=0.048$ ). At the second examination, shortening of P1 latencies was registered (REs/LEs  $98.3 \pm 2.4/102.7 \pm 4.5$  ms;  $p < 0.001$ ). The dynamics of latency shortening for REs/LEs were  $17 \pm 1.3/15.1 \pm 3.1$  ms, with insignificant inter-eye difference ( $p=0.271$ ). The dynamics of remyelination correlated with serum methanol ( $r=-0.588$ ;  $p < 0.001$ ), arterial pH ( $r=0.339$ ;  $p=0.040$ ), and concentration of carbohydrate-deficient transferrin ( $r=-0.411$ ;  $p=0.011$ ). Remyelination occurred in cases of mild or moderate damage of myelin sheaths; no improvement of conduction was found in severe cases. **Conclusion:** The dynamics of remyelination correlated with the degree of acidosis and severity of poisoning. Chronic alcohol abuse had a negative effect on remyelination dynamics.

## 101. Efficacy of isosorbide dinitrate as an antidote for cyanide poisoning in rabbits depending on the timing of treatment

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**Objective:** To evaluate the efficacy of isosorbide dinitrate as an antidote for cyanide poisoning in rabbits and the effect of the timing of treatment. **Methods:** A comparative *in vivo* study using male  $3000 \pm 200$  g New Zealand White rabbits, randomly divided into 4 groups. The rabbits were poisoned by intravenous lethal doses of potassium cyanide (1 mg/kg); in a previous study we demonstrated that these cyanide doses caused a high mortality (5/6) within minutes (median 10 min). The animals in the different groups were treated intravenously with isosorbide dinitrate at a dose of 50 mcg/kg at 1, 3, 5 or 7 minutes after the poisoning, respectively. The primary outcome was short-term survival up to 30 minutes. Other outcomes that were examined included time to death, clinical score, mean blood pressure, pulse, blood pH, and blood lactate concentrations. **Results:** There were 24 rabbits in 4 groups of 6. All animals (6/6) in the group treated 1 minute after poisoning survived. Five rabbits out of 6 from each of the other groups survived. The time to death of rabbits that died (one in each group treated after 3, 5 and 7 minutes) was within the range of 8–13 minutes after poisoning. All animals collapsed shortly after poisoning accompanied by disturbed vital signs (blood pressure increased and heart rate decreased). Lactic metabolic acidosis developed further; average peak blood lactate concentrations were 15.5–19.0 mmol/L at 10 minutes after poisoning. The treated rabbits gradually improved in all measured parameters. Recovery was faster in the animals that were treated 1 and 3 minutes after poisoning. Blood pH and lactate concentrations improved slowly compared to the clinical score and the hemodynamic parameters.

**Conclusion:** Isosorbide dinitrate improves survival of rabbits poisoned with lethal doses of potassium cyanide when given even up to 7 minutes after poisoning. Recovery of the animals was faster when treated early after poisoning (1–3 minutes). Delayed recovery of the animals treated later is probably secondary to the accumulated metabolic injury, mainly lactic acidosis. Isosorbide dinitrate shows potential as an effective antidote for cyanide poisoning in a realistic time window.

## 102. Hydrofluoric acid: an *in vitro* experiment in a 3D human airway reconstructed epithelia

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**Objective:** Hydrofluoric acid (HF) is very corrosive and hazardous for human exposure.[1] Inhalation of hydrofluoric acid can be fatal but few data are available to understand how hydrofluoric acid damages lung. **Methods:** We designed an experiment to explore the effect of HF on MucilAir™ a unique 3D Human Airway Epithelia reconstructed *in vitro*. [2] For the study 100  $\mu$ l of HF was applied on the epithelia for 20 minutes; the concentrations tested were 0.15, 0.75, 1.5, 7.5, 15, 75 and 150 mM. The following endpoints were analyzed: morphology, tissue integrity monitoring (TEER), lactate dehydrogenase (LDH) release quantification, Cilia Beating Frequency (CBF) and histology. **Results:** For concentrations up to 1.5 mM of HF, no toxic effects were detected by all the endpoints measured. At concentrations of 7.5 mM and above, damage to epithelia were observed. The TEER dropped significantly, the pseudo-stratified structure was altered and only the basal cell layer was present. Cilia beating frequency was reduced, however, based on TEER analysis, damage caused by HF below 7.5 mM could be repaired 7 days after exposure, and the CBF values recovered despite some variations at earlier time-points, except when HF was used above 75 mM. HF at 75 mM and above caused severe damage to epithelia, which was not reversible. Histology clearly showed that the pseudo-laminate structure including the three cell types was well maintained for inspection and treatment with HF at 1.5 mM. HF 15 mM contact induced an abnormal structure with the presence of a single layer of basal cells. This is perfectly in line with the high value of TEER found to Day 7. From 15 to 150 mM strong and non-reversible toxicity was observed. **Conclusion:** The MucilAir™ model allows characteristic damages induced by HF and confirms that a low concentration of hydrofluoric acid can induce irreversible cellular damage. The model could be of interest to evaluate the benefit of early decontamination and treatments in further studies.

## References

- [1] Tsonis L, Hantsch-Bardsley C, Gamelli RL. Hydrofluoric acid inhalation injury. *J Burn Care Res.* 2008;29:852–855.
- [2] Baxter A, Thain S, Banerjee A, et al. Targeted omics analyses, and metabolic enzyme activity assays demonstrate maintenance of key mucociliary characteristics in long term cultures of reconstituted human airway epithelia. *Toxicol In Vitro.* 2015;29:864–875.

### 103. Hyperbaric oxygen protects neurotrophic activity of carbon monoxide-exposed astrocytes

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**Objective:** Carbon monoxide (CO) causes neuronal and glial apoptosis that can result in delayed neurological symptoms. Recently we reported that CO/normoxia caused a progressive decline of viability and mitochondrial function accompanied by caspase and calpain activation.[1] Impairment in astrocyte function was reduced time-dependently by hyperbaric, not normobaric, oxygen. Due to the central role of astrocytes in maintaining neuronal function by offering neurotrophic support we investigated the toxic effects of CO/normoxia on intrinsic neurotrophic activity in these cells and evaluated possible protective influence of oxygen treatment against CO poisoning. **Methods:** Cultured rat astrocytes were exposed to 3000 ppm CO in air for different time periods (0.5–24 hours) followed by 24 hours of normoxia. Following an 8 hour exposure to CO that significantly affected astrocytic cellular function the cultured cells were exposed during 24 hours of normoxia for 1 hour in different time periods (0–7 hours) after CO to 100% normobaric oxygen (NBO) or 100% oxygen at a pressure of 3 bar (HBO). Real-time polymerase chain reaction (PCR) was performed to examine the expression of nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3). Specific two-site enzyme immunoassays were utilized to determine protein synthesis and secretion of the examined neurotrophins. **Results:** CO/normoxia caused a progressive decline of gene expression, synthesis and secretion of NGF, BDNF and NT-3 with different intensity. Maximal response occurred after 8 hours in CO. Subsequent 1 hour treatment with oxygen disclosed pressure- and time-dependent efficacy in restoring astrocytic neurotrophic activity. The protective effect was evident when cells were exposed to HBO 1–5 hours after CO but not when exposed to HBO immediately after CO exposure. A diminished efficiency of HBO in enhancement of neurotrophin synthesis was observed 7 hours after CO exposure. In contrast, NBO had no protective influence on CO-poisoned cells. **Conclusion:** The neuroprotective role of oxygen therapy in CO-exposed astrocytes is pressure- and time-dependent. In addition to preventing mitochondrial dysfunction and apoptotic processes our results indicate that HBO, but not NBO, restores astrocytic neurotrophic support that may dictate the short- and long-term neuronal survival and the maintenance and retraction of synaptic connections. To prevent the occurrence of late neuropsychological sequelae our study opens the way to consider time and pressure regimen of oxygen therapy in clinical management of CO poisoning.

### References

- [1] Jurič DM, FINDERLE Ž, ŠUPUT D, et al. The effectiveness of oxygen therapy in CO poisoning is pressure- and time-dependent. *Toxicol Lett.* 2015;233:16–23.

### 104. A novel, fluorescence-based method to detect effects of novel psychoactive substances (NPS) on neurotransmitter re-uptake transporters

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**Objective:** Prevalence of drug use, including novel psychoactive substances (NPS), is high and new substances are emerging yearly. Most drugs are well-known to affect the function of neurotransmitter reuptake transporters. Often, this is investigated using radioactive assays, requiring specific laboratory facilities. As the demand for rapid methods to investigate the potency of substances affecting neurotransmission is increasing, we used a novel fluorescence-based high-throughput method to investigate effects of NPS on re-uptake transporters for dopamine (DAT), norepinephrine (NET), and serotonin (SERT). **Methods:** Human embryonic kidney cells (HEK 293, kindly provided by Roche) expressing human neurotransmitter re-uptake transporters (hDAT, hNET or hSERT) were used to determine the effect on neurotransmitter uptake during a 30 minute exposure to several drugs and measure their half maximal inhibitory concentration (IC<sub>50</sub>). Frequently used common drugs and NPS were selected: cocaine, amphetamine, 4-fluoroamphetamine, methoxetamine, para-methoxymethamphetamine (PMMA), 2C-B, 2C-B-NBOMe and 2C-I-NBOMe. Uptake was determined using a fluorescent substrate that mimics dopamine, norepinephrine and serotonin. Uptake of the substrate increases intracellular fluorescence, which was measured over time with a microplate reader. **Results:** All drugs inhibited monoamine transporter function in a concentration-dependent manner. hDAT and hNET were most potently inhibited by cocaine, amphetamine and 4-fluoroamphetamine (IC<sub>50</sub> ~1–5 μM), while 2C-B was a weak inhibitor (IC<sub>50</sub> >100 μM). hSERT was most potently inhibited by cocaine, methoxetamine and the NBOMes (IC<sub>50</sub> ~2–5 μM), while amphetamine and 4-fluoroamphetamine were weak inhibitors. PMMA strongly inhibited hNET (IC<sub>50</sub> 6 μM) and less potently inhibited hDAT and hSERT (IC<sub>50</sub> 43 and >100 μM). **Conclusion:** Our data show that the fluorescence-based assay can be used to rapidly determine effects of substances on the function of neurotransmitter reuptake transporters, without the need of a specially equipped laboratory. In addition, this method allows for measurements over time, in contrast to endpoint measurements. This can be useful to investigate the effect of successive exposures, for example, when examining a candidate drug for undue drug-induced transporter effects.

## 105. Variability of neurobehavioral toxicity of naphyrone, a new synthetic cathinone, with acute or binge administration

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**Objective:** Naphyrone is a new psychoactive substance and a cathinone derivative. It was reported to be used by approximately 2% of recreational drug users and is frequently present in “bath salts”. Scarce data are available regarding its toxicity, pharmacokinetics and effects on brain monoamines. Our objectives were to study naphyrone-related effects on behavior and brain monoamine content in mice according to two administration modalities (acute and binge) mimicking its use in humans. **Methods:** An experimental study in Swiss mice of naphyrone-induced effects after acute and repeated administration (binge) on the locomotor activity, anxiety (openfield), resignation (forced swimming), memory (Y-maze), hedonic status (sucrose consumption) and investigation of naphyrone-induced effects on monoamines in the prefrontal cortex. Plasma naphyrone concentrations were measured using high performance liquid chromatography-mass spectrometry (HPLC-MS) and brain monoamine concentrations using HPLC coupled to fluorometry. For each animal and each time, we calculated the difference between the parameter value at that time and baseline and the area under the curve of its time course. Comparisons were performed using two-way ANOVA followed by post-tests using Bonferroni correction. Pharmacokinetics (PK) was modeled and parameters calculated using WinNonlin<sup>®</sup> software. **Results:** Naphyrone-induced dose-dependent stimulation of locomotor activity that appeared more marked and prolonged than methylenedioxypropylvalerone (MDPV)- and cocaine-related effects (used as positive controls), additionally increasing after binge administration ( $p < 0.001$ ). Significant increase in the distance walked at the periphery of the openfield was observed up to 24 hours post-injection ( $p < 0.001$ ), corresponding to the behavior compensation of enhanced fear. During binge administration (3 times per day, 3 successive days), increased locomotor effects at day 3 (after the 9th injection) in comparison to day 1 (after the 1st injection) supported naphyrone-induced hyper-sensitization process. Similarly, significant effects were observed on mice depression ( $p < 0.0001$ ) and memory ( $p < 0.005$ ) but not on hedonic status. Significant dose-dependent increase in aggressively social relationships was also reported among naphyrone-treated mice ( $p < 0.001$ ). The neurochemical study revealed significant increase in dopamine and norepinephrine concentrations in the prefrontal cortex, without significant modifications in serotonin concentrations. This monoamine profile was similar after repeated naphyrone administration. The naphyrone pharmacokinetic profile was described after acute and binge administration and effects correlated to plasma concentrations. **Conclusion:** Neurobehavioral disorders induced by acute and repeated naphyrone administration mainly consist of the stimulation of locomotor activity. The increase in the cortical dopamine concentrations may suggest an addictive potential that should be further investigated.

## 106. Acute behavioral toxicity and addictive liability of the synthetic cathinone 3,4-methylenedioxypropylvalerone (MDPV) in the rat

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**Objective:** 3,4-Methylenedioxypropylvalerone (MDPV), a synthetic cathinone with toxicity and high abuse potential, has been increasingly used over the last five years. To date, few experimental studies have investigated MDPV-related behavioral effects. We studied MDPV-related neurobehavioral effects in rats in various modalities of administration, mimicking human use. **Methods:** An experimental study in Sprague-Dawley rats investigating MDPV-induced effects on the locomotor activity, anxiety (openfield), resignation (forced swimming), memory (Y-maze), hedonic status (sucrose consumption) and brain neurochemistry (monoamines content in the prefrontal cortex), using three different administration patterns including acute (3 mg/kg intraperitoneal injection [IP]), binge-like (MDPV 3 mg/kg IP, 3 times per day, 3 days) and prolonged treatment (MDPV 1 mg/kg IP, 10 days). Plasma concentrations of MDPV and its two major metabolites were measured using liquid chromatography coupled to high-resolution mass spectrometry. Brain monoamine concentrations were measured using high-performance liquid chromatography (HPLC) coupled to fluorometry. For each animal and each time, we calculated the difference between the parameter value at that time and baseline and the area under the curve of its time course. Comparisons were performed using two-way ANOVA followed by post-tests using Bonferroni correction. **Results:** Acute MDPV administration was responsible for locomotor hyperactivity with onset of stereotypies, significant decrease in anxiety, anhedonic status, and memory impairment ( $p < 0.05$  for each neurobehavioral measurement). Following binge-like MDPV administration, tolerance to immediate locomotor effects after drug withdrawal and significant decrease in anxiety, hedonic status and food consumption were observed ( $p < 0.05$  for each neurobehavioral measurement). Increase in the prefrontal cortex serotonin concentrations occurred, in accordance with the observed behavioral effects. Prolonged MDPV administration resulted in tolerance development after one week of drug withdrawal. **Conclusion:** Our results suggest MDPV-induced marked neurobehavioral effects in the rat with the development of tolerance after binge-like and prolonged repeated administration.

## 107. A bifunctional and peptide-based opioid agonist-nociceptin antagonist ligand for treatment of pain: is the benefit-to-neurorespiratory toxicity ratio improved compared to the usual opioids?

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**Objective:** Pain is a key public health concern, affecting one in five adults across Europe (ca. 75 million people). To date, morphine and tramadol are the two major agents used to treat acute and neuropathic pain, respectively. In order to simultaneously address these two types of pain, a bifunctional hybrid (KGNOP1) was developed associating a peptide-based opioid agonist (KGOP1) to a nociceptin antagonist. Our objective was to investigate KGNOP1-induced anti-nociceptive and anti-hyperalgesic effects in comparison to its related respiratory effects in Sprague-Dawley rats, focusing on determining their time-course and dose-effect relationships in comparison to the reference treatments. **Methods:** The anti-nociceptive effects were determined using the hot plate (kept at a temperature of 52°C, maximum latency period to paw lick or paw brisk shaking set at 60s), the anti-hyperalgesic effects using the cold plate (kept at a temperature of 4°C, number of paw withdrawal in rats with chronic constriction injury-induced neuropathic pain) and the respiratory effects using plethysmography (measurement of inspiratory and expiratory times and tidal volume). We determined the dose-effect relationships for each tested drug (KGNOP1, KGOP1, morphine, tramadol, and solvent) according to the investigated effect. To permit the simultaneous analysis of the effect of time and treatments on the different parameters, we calculated for each animal and for each studied parameter, the area under the curve (AUC) from T0 to the completion of the measurement. For each parameter, we compared the AUCs using Kruskal-Wallis tests between the studied groups. The effective doses 50% (ED<sub>50</sub>) were determined using sigmoidal modeling. **Results:** KGNOP1 was responsible for dose-dependent anti-nociceptive effects more marked and lasting longer than morphine ( $p < 0.05$ ), initial and prolonged anti-hyperalgesic effects in comparison to tramadol ( $p < 0.05$ ), but dose-dependent increase in inspiratory time greater than morphine ( $p < 0.05$ ). Additionally, the respiratory depression induced by KGNOP1 was more marked than with its opioid part, KGOP1, alone ( $p < 0.05$ ). The ED<sub>50</sub> regarding the anti-nociceptive effects were calculated at 0.35 μmol/kg with KGNOP1 and 14.7 μmol/kg with morphine while ED<sub>50</sub> regarding the respiratory effects were at 0.43 μmol/kg with KGNOP1 and 16.2 μmol/kg with morphine, allowing attribution to KGNOP1 of a poor therapeutic margin of 1.23, similar to morphine. **Conclusion:** KGNOP1-induced anti-nociceptive and anti-hyperalgesic activities are greater than those of the tested reference treatments; however KGNOP1-related respiratory toxicity appears too important to allow its consideration for any therapeutic application.

## 108. The disposition of cocaine and its metabolites in biological matrices following controlled administration in volunteers

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**Objective:** Previous studies describing the pharmacokinetics of cocaine and its metabolites focus on plasma and urine sample analysis. There are limited data on cocaine/metabolite pharmacokinetics and disposition in whole blood, oral fluid, sweat and/or hair. Analysis of these matrices is particularly relevant to forensic investigations and workplace drug-testing as they are easy to store and transport. The study aimed to describe the disposition and pharmacokinetics of cocaine and its metabolites in these matrices. **Methods:** After informed consent, 7 healthy drug-naive male volunteers (25–40 years) insufflated a single 100 mg dose of pharmaceutical-grade cocaine hydrochloride. Whole blood, plasma, oral fluid and palm sweat were sampled regularly over the first 6 hours and on days 2 and 3. Head hair samples were taken at baseline and 30, 60 and 90 days. Samples were stored at -20°C until analysis using ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) for cocaine, benzoylecgonine (BZE), ecgonine methyl ester (EME); hair samples were also analysed for norcocaine. **Results:** Cocaine was detected in whole blood, plasma and oral fluid samples at the first collection (5 mins) and BZE/EME in samples collected at the second collection (10 mins). There was a significant correlation between whole blood and plasma cocaine for BZE and EME ( $r^2$  0.860–0.963,  $p < 0.0001$ ). Calculated maximum serum concentration (C<sub>max</sub>) for cocaine was 417.1 ng/mL in whole blood and 450.3 ng/mL in plasma. The time to reach the maximum serum concentration (T<sub>max</sub>) was 21 and 27 minutes, respectively, with half-life 1.3 and 1.5 hours, respectively. Calculated C<sub>max</sub> for BZE was 386.1 ng/mL (whole blood) and 414.1 ng/mL (plasma); T<sub>max</sub> was 145 and 180 minutes, respectively. Calculated C<sub>max</sub> for EME was 135.1 ng/mL (whole blood), 118.8 ng/mL (plasma); T<sub>max</sub> 137 and 120 minutes, respectively. Mean C<sub>max</sub> whole blood:plasma ratios were 0.90 for cocaine, 0.94 for BZE and 1.13 for EME. Cocaine and BZE were first detected in palm sweat 1 hour after cocaine administration and EME at 2 hours; they remained detectable for 24 and 48 hours for EME and cocaine/BZE, respectively. Cocaine, BZE, EME and norcocaine were detected in hair samples at all time points. **Conclusion:** The whole blood:plasma cocaine and metabolite ratios neared unity. Whole blood/plasma cocaine and metabolite kinetics suggest that both matrices are suitable for forensic and clinical sampling. The time course of detection of cocaine/metabolites in oral fluid and palm sweat will aid interpretation of forensic and work-place testing. Detection of norcocaine in hair samples confirms endogenous cocaine/metabolite inclusion into hair rather than surface contamination and *ex vivo* metabolism.

## 109. Polyvinylpyrrolidone-coated iron oxide nanoparticles (PVP-Fe<sub>3</sub>O<sub>4</sub>NPs): toxicological profile evaluation in human brain cells

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**Objective:** Magnetic iron oxide nanoparticles (IONPs) as magnetite ( $\text{Fe}_3\text{O}_4\text{NPs}$ ) have attracted extensive interest due to their superparamagnetic physicochemical properties in biomedical (i.e. brain-targeted drug, magnetic resonance imaging, contrast agents) and industrial fields (i.e. audio speakers, position sensing, water purification).  $\text{Fe}_3\text{O}_4\text{NPs}$  can reach the central nervous system (CNS) independent of administration route. Considering the role of astrocytes in iron (Fe) homeostasis and protection of brain cells against metal toxicity, exposure to  $\text{Fe}_3\text{O}_4\text{NPs}$  may be a risk due to Fe ion release leading to a disruption of normal iron metabolism/homeostasis in the brain - a characteristic hallmark resembling that of several neurodegenerative disorders. **Methods:** Effects induced by polyvinylpyrrolidone (PVP)- $\text{Fe}_3\text{O}_4\text{NPs}$  ( $\varnothing$  20 nm) were assessed on D384 astrocyte and SH-SY5Y neuronal cells after 4, 24 and 48 hours at increasing concentrations (1–100  $\mu\text{g}/\text{mL}$ ) by evaluating the following biological functions: mitochondrial activity (MTT assay); cell membrane integrity (calcein-AM/PI-staining); cell morphology (phase-contrast microscopy); and intracellular PVP- $\text{Fe}_3\text{O}_4\text{NP}$  accumulation (Prussian blue-staining). **Results:** PVP- $\text{Fe}_3\text{O}_4\text{NPs}$  induced dose- and time-dependent alterations of mitochondrial function in D384; 25–30% cell viability decrease was observed early (4 h) from 25 to 100  $\mu\text{g}/\text{mL}$ . Cytotoxicity was more pronounced after prolonged exposure with 35–55% cell death after 24 h (10–100  $\mu\text{g}/\text{mL}$ ) and 25–75% after 48 h (1–100  $\mu\text{g}/\text{mL}$ ). SH-SY5Y were less susceptible than D384. Cytotoxicity was observed after 48 h only with 35–45% viability decrease (10–100  $\mu\text{g}/\text{mL}$ ). No effect on membrane integrity was observed in both CNS cell types at all doses and time-points considered. D384 showed morphological alterations (roundish cells) at the highest doses (50–100  $\mu\text{g}/\text{mL}$ ) after 48 h, while no effect was observed in SH-SY5Y. Dose- and time-dependent PVP- $\text{Fe}_3\text{O}_4\text{NP}$  accumulation was detected in both cell types. Blue spots in D384 were visible at  $\geq 10 \mu\text{g}/\text{mL}$  after 4 h and increased at higher doses (25–100  $\mu\text{g}/\text{mL}$ ), and in SH-SY5Y they were detected at  $\geq 25 \mu\text{g}/\text{mL}$ . **Conclusion:** PVP- $\text{Fe}_3\text{O}_4\text{NPs}$  alter mitochondrial function only, with astrocytes being more susceptible than neurons. Critical doses are 25  $\mu\text{g}/\text{mL}$  after 4 h and 1  $\mu\text{g}/\text{mL}$  after 48 h for D384 and 10  $\mu\text{g}/\text{mL}$  after 48 h for SH-SY5Y. Fe accumulates in a dose- and time-dependent manner mainly in astrocytes. In summary, mitochondrial effects of PVP- $\text{Fe}_3\text{O}_4\text{NPs}$  in cerebral cells could raise health concerns based on the possibility that cellular IONP overload may trigger adverse cellular responses by releasing Fe ions (especially in astrocytes) compromising the normal functions of the CNS. **Acknowledgements:** Italian Ministries of Health, Research and Education; and ENI S.p.A. Div-R&M.

## 110. Lack of symptoms following a large combined carbamazepine and quetiapine overdose: the role of enzyme induction by carbamazepine

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**Objective:** Carbamazepine is a potent inducer of cytochrome P450 (CYP) 3A4 and P-glycoprotein. Induction is known to reduce plasma concentrations of other CYP3A4 metabolized drugs when these are taken in normal therapeutic doses. We report the same effect following an acute overdose of two CYP3A4 metabolized drugs taken in large quantities. **Case report:** A 32-year-old female with a year-long history of anorexia presented to the emergency department 2 hours after an acute overdose of 14 g carbamazepine and 10.8 g quetiapine. Past medical history included myxedema, epilepsy and depression and medications were

levothyroxine (150 mcg/day), carbamazepine (300 mg/day) and quetiapine (600 mg/day). Overdose was reported by the patient and confirmed by psychiatric contact personnel. At the time of presentation she was without symptoms, including normal electrocardiogram (ECG). She was treated with one dose of activated charcoal and admitted to the cardiology department for cardiac monitoring and close observation. The Danish Poison Information Center was consulted, and advice was given to expect severe symptoms and to administer multiple doses of activated charcoal (MDAC). No symptoms developed within 48 hours of observation. Plasma quetiapine concentrations 6.5, 14.5 and 20 hours after ingestion were 230, 27 and  $<13 \text{ nmol}/\text{L}$  (therapeutic range 50–650 nmol/L), respectively, giving an estimated half-life of 2.5 hours (normal range 4.9–8.4 hours).[1] Serum carbamazepine concentrations 6.5, 10.5, 14.5, 20 and 35 hours after ingestion were 37, 33, 21, 16 and 7  $\mu\text{mol}/\text{L}$  (therapeutic range 20–50  $\mu\text{mol}/\text{L}$ ), respectively, giving an estimated half-life of 11.5 hours (normal range 10–20 hours). **Conclusion:** The carbamazepine-induced CYP3A4 activity may have markedly reduced the intoxication symptoms in this case of a confirmed large overdose of carbamazepine and quetiapine. Both peak concentration and the half-life of quetiapine were markedly reduced and quetiapine never reached toxic plasma concentrations, even with this large dose. The MDAC may have contributed to the lower peak concentration of both drugs, but the rapid elimination, low bioavailability and lack of symptoms following the large quetiapine ingestion is likely to be a consequence of carbamazepine CYP3A4 induction.[2]

## References

- [1] Isbister GK, Friberg LE, Hackett LP, et al. Pharmacokinetics of quetiapine in overdose and the effect of activated charcoal. *Clin Pharmacol Ther.* 2007;81:821–827.
- [2] Grimm SW, Richtand NM, Winter HR, et al. Effects of cytochrome P450 3A modulators ketoconazole and carbamazepine on quetiapine pharmacokinetics. *Br J Clin Pharmacol.* 2006;61:58–69.

## 111. Acrylamide poisoning with long-term neurological consequences

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**Objective:** Acrylamide and its polymer, polyacrylamide, are widely used in the water treatment, papermaking, electrophoresis gels, dyes, cosmetics and textile industries. International organizations have classified acrylamide as a potential carcinogenic and neurotoxic agent.[1,2] **Case report:** A 31-year-old woman with no relevant personal history or toxic habits, accidentally inhaled acrylamide at work. Immediately after exposure, she suffered a 45-minute episode of dizziness, loss of strength, tingling in the arms and feet, blurred vision, slurred speech, drowsiness and respiratory difficulties. The patient was treated at the emergency department of a nearby hospital, remaining under observation for 48 hours with monitoring, fluids and oxygen therapy. After discharge, she continued to suffer from progressive deterioration for two years, with asthenia, headache, cognitive disorders, dizziness, hypoesthesia, paresthesia, dry eye and visual accommodation problems. Study by the Clinical Toxicology Unit, University of Valladolid found symptoms compatible with cerebellar ataxia associated with bitemporal hemianopsia. The panel of tests



performed included: standard biochemistry, uric acid, lactate dehydrogenase, creatine kinase, total proteins, C-reactive protein, rheumatoid factor, ammonia, glutamic acid, hormones (PTH, TSH, T3, T4, cortisol, FSH, LH, ACTH, prolactin, progesterone, testosterone), antibodies (ANA, anti-SSA, anti-SS, anti-transglutaminase antibodies, ANCA, anti-Yo, anti-Hu, anti-Tr, anti CCDI antibodies), vitamins (25-hydroxyvitamin D, vitamin B902, folic acid, vitamin E), serology (herpes simplex, cytomegalovirus, Epstein Barr, Borrelia, human immunodeficiency virus, human T-lymphotropic virus type 1), tumor markers (CEA, CA12.5, CA 19.9, alpha fetoprotein), metals (copper, lead), ceruloplasmin, angiotensin converting enzyme (ACE) and urine (fractionated porphyrins, mercury, and lead). All results were negative or within normal parameters. Brain and spine computerised tomography and magnetic resonance imaging with and without contrast, magnetic resonance myelography and electromyography showed no significant alterations. **Conclusion:** The cause-effect relationship between exposure to acrylamide and the onset of symptoms and the absence of an identifiable organic cause suggests the neurological damage in this case was due to acrylamide poisoning.

## References

- [1] Exon JH. A review of the toxicology of acrylamide. *J Toxicol Environ Health B Crit Rev.* 2006;9:397–412.
- [2] Pennisi M, Malaguarnera G, Puglisi V, et al. Neurotoxicity of acrylamide in exposed workers. *Int J Environ Res Public Health.* 2013;10:3843–3854.

## 112. The challenge of unknown chemical exposure

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**Objective:** Chemical injury on skin is not always obvious. Unlike strong acids, hydrofluoric acid burns do not present with apparent coagulum, but the acid penetrates deeply into tissues to cause severe injuries.[1,2] **Case report:** A 35-year-old male presented with a painful skin rash on the legs two hours after being splashed with a clear fluid while cycling past a street populated by small-sized factories. The pH of the unknown liquid on his jeans was measured to be 1 using litmus paper. He was managed as for an ordinary acid corrosive injury and the burn was dressed with antibiotic ointment, however he later developed severe local pain, deep into bone, and after toxicology consultation it was thought that the fluid could have been hydrofluoric acid. The patient had some improvement after local application of calcium gluconate, but the wound required repeated surgical debridement and skin grafting due to extensive necrotic lesions. Fluoride ion was detected in the jeans by ion exchange chromatography. **Conclusion:** Emergency physicians should be aware that concentrated hydrofluoric acid can induce deep tissue destruction due to penetration of fluoride ion, but does not burn clothes due to its weak acidity. These combined characters might be the clue for differential diagnosis of acid corrosive injury.

## References

- [1] Dinis-Oliveira RJ, Carvalho F, Moreira R, et al. Clinical and forensic signs related to chemical burns: a mechanistic approach. *Burns.* 2015;41:658–679.

- [2] Stuke LE, Arnoldo BD, Hunt JL, et al. Hydrofluoric acid burns: a 15-year experience. *J Burn Care Res.* 2008;29:893–896.

## 113. Risks related to mineral oils after accidental injection of veterinary vaccines: prospective study at the Poison Control Centre of Angers

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**Objective:** The accidental injection of veterinary vaccines (VV) causes septic complications and persistent functional impairment.[1,2] The presence of mineral oil (MO) used as an excipient appears to result in more frequent complications. The objective of this prospective study was to demonstrate that the presence of MO in VVs increases the risk of septic and functional complications. **Methods:** A prospective study of cases of injection of VVs compiled by the Poison Control Centre of Angers between 2007 and 2014. The assessment criteria selected were: septic complications, functional impairment at one month and surgery. The explanatory variables were: age, sex, contaminated syringe, pressure injection, site of injury and presence of mineral oil. The statistical study is based on a multivariate analysis of the data. **Results:** In total 266 cases of VV injection were identified between 2007 and 2014. In 89% of cases the circumstances were professional and in 58% of cases occurred while vaccinating poultry. VVs contained MO in 62% of cases. The site of the injury was the hand in 77% of cases. Out of the 266 patients, 72 (i.e. 27%) developed complications such as abscess, phlegmon, tenosynovitis, arthritis, lymphangitis, and 46 required surgery. At the one month follow up, 45 patients had a persistent functional impairment. The presence of MO in the VVs increases the risk of septic complications (adjusted OR at 4.4;  $p < 0.002$ ). MOs were also associated with a significantly greater number of surgical procedures and persistent functional impairment. **Conclusion:** This prospective study reveals a high frequency of septic complications with VV injections. The presence of MO significantly increases the septic complications and accrues the surgical procedures and the persistence of a functional impairment. An accidental injection of this type of vaccine could require surgery despite appropriate treatment and early antibiotic therapy. A national prospective protocol organised in 2015 by a group of experts (Poison Centres, Veterinary Medicines Agency and the French Agency for Food, Environmental and Occupational Health & Safety [ANSES]) should ultimately allow the proposal of preventive and corrective measures.

## References

- [1] Woodward KN. Adverse reactions in humans to veterinary medicinal products. *J Vet Pharmacol Ther.* 2005;28:185–201.
- [2] Couzens G, Burke D. Veterinary high pressure injection injuries with inoculation for larger animals. *J Hand Surg Br.* 1995;4:497–499.

## 114. Severe poisoning after ingestion of chloroform

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**Objective:** Poisoning due to chloroform ingestion is rare and few cases have been reported. The classic features of chloroform toxicity include rapid loss of consciousness, respiratory depression and delayed hepatotoxicity. We describe a case of ingestion with transaminitis, severe gastrointestinal inflammation and hypoglycaemia. **Case report:** A 30-year-old female ingested 20–30 mL of 99% chloroform. At the scene, vital signs were Glasgow Coma Scale (GCS) 3, heart rate (HR) 100 bpm, unrecordable blood pressure (BP) and respiratory rate (RR) 20/min. On arrival to the emergency department she was intubated for decreased GCS, bradypnoea and desaturation. Laboratory investigations showed blood glucose 9.7 mmol/L, bilirubin 16 µmol/L (<15), aspartate transaminase (AST) 62 IU/L (<35), alanine transaminase (ALT) 24 IU/L (<30) and white cell count of  $34 \times 10^9/L$ . The ALT began to rise at 36 hours and peaked at 1283 IU/L at 72 hours. International Normalized Ratio (INR) began to rise at 14 hours, peaking at 2.3 by 36 hours. The bilirubin and AST peaked at 67 hours post-ingestion at 64 µmol/L and 734 IU/L, respectively. Intravenous acetylcysteine was commenced at 42 hours, as per the protocol for paracetamol toxicity, and was continued for 72 hours until liver function tests (LFTs) peaked and were declining.[1] Electrolytes, renal function, chest X-ray and electrocardiogram remained normal throughout. She had one episode of hypoglycaemia at 16 hours (3.7 mmol/L), which resolved with intravenous dextrose. Contact dermatitis was noted on the face and upper back, caused by excoriation from drooling saliva and vomitus. A chest and abdominal computerised tomography (CT) scan showed extensive small and large bowel oedema and thickening consistent with extensive toxin-induced enteritis and colitis. An upper gastrointestinal endoscopy confirmed oesophageal erosions and severe erosive gastritis. She was kept nil by mouth and treated with proton pump inhibitors, sucralfate and total parenteral nutrition for 4 days. The patient was discharged home on day 9, following psychiatric assessment, by which time the dermatitis had resolved, she was tolerating oral intake and her LFTs were near normal. Chloroform was detected in blood using headspace gas chromatograph mass spectrometry. **Conclusion:** Our case demonstrates that chloroform-induced hepatotoxicity occurs about 36 hours post-ingestion, similar to paracetamol hepatotoxicity. Chloroform can also lead to contact dermatitis, severe gastritis and entero-colitis. Recovery occurred with good supportive care.

### Reference

- [1] Dell'Aglio DM, Sutter ME, Schwartz MD, et al. Acute chloroform ingestion successfully treated with intravenously administered N-acetylcysteine. *J Med Toxicol.* 2010;6:143–146.

## 115. Methyl ethyl ketone peroxide toxicity treated with acetylcysteine

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**Objective:** Methyl ethyl ketone peroxide (MEKP) is a highly reactive substance, often used as a fiberglass fixing agent. Although a rare, mainly unintentional, poisoning it is highly toxic causing corrosive effects in the gastrointestinal tract, hepatic necrosis, renal impairment and cardiovascular collapse. We report a case of MEKP toxicity managed with acetylcysteine infusion and supportive care. **Case report:** A 57-year-old male presented to the emergency department of a metropolitan hospital with profuse, watery diarrhoea and diaphoresis. He had ingested a mouthful of liquid, whilst working on his boat, which he believed to be water but was in fact MEKP. Vital signs on arrival were heart rate 120 bpm, blood pressure 170/90 mmHg, respiratory rate 30/min and oxygen saturations 100% on a non-rebreather mask. His initial venous blood gas showed a compensated metabolic acidosis with a lactate of 6.0 mmol/L. His haemoglobin was 210 g/L which was thought to reflect haemoconcentration from intravascular volume depletion. Initial liver function tests (LFTs) were alanine transaminase (ALT) 55 U/L, aspartate transaminase (AST) 91 U/L and International Normalized Ratio (INR) 1.0. Approximately 12 hours post-ingestion his LFTs worsened with ALT 637 U/L, AST 551 U/L and INR 1.3. Following consultation with the poisons information centre, acetylcysteine was commenced. Over the next 24 hours transaminases continued to rise with ALT peaking at 761 U/L and AST 576 U/L; INR remained slightly elevated at 1.3. The patient also complained of throat pain and his oral intake decreased. A chest computerised tomography (CT) scan was performed which excluded oesophageal perforation but suggested some colonic thickening based on the small section of large bowel visible on the scans. He continued to have diarrhoea for 48 hours post-ingestion while his transaminases were decreasing and INR was 1.1. At 72 hours post-ingestion acetylcysteine was stopped. On telephone follow up at 14 days post-ingestion he was clinically well. AST was within normal limits but ALT remained slightly elevated at 89 U/L (reference <51). MEKP was confirmed in blood with headspace gas chromatography-mass spectrometry. **Conclusion:** The case confirms the unintentional ingestion of this highly toxic volatile substance. Despite a small ingestion it caused hepatotoxicity and gastrointestinal injury.

## 116. Risks from and concerns about sodium fluoroacetate (1080): a review of enquiries to the New Zealand Poisons Centre

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**Objective:** The rodenticide sodium fluoroacetate (1080; usually as 0.15% baits) has been used for decades in New Zealand for controlling possums and other pests to protect forests and native bird species. The aim of this study was to review enquiries to the

National Poisons Centre (NPC) regarding 1080, to help clarify public concerns and possible risks from its continuing use. **Methods:** A review was conducted of all telephone enquiries to the NPC regarding 1080 for the five year period between January 2010 and December 2014. The enquiries were classified in terms of relevant features such as caller background, "victim" (human or animal), and site and route of exposure where relevant. Our descriptions and assessments of the incidents were also reviewed. **Results:** There were 102 enquiries, only 25 of which related to actual, probable or possible exposure, 11 involving humans and 14 animals, the latter mainly dogs. These human exposure enquiries mainly involved possible contact via aerial drops (4 incidents, 6 enquiries), but also included one occupational exposure and a possible intentional ingestion. None involved children. Ten further enquiries were from callers concerned about potential 1080 exposure but the description of events suggested this would have been very unlikely. The majority ( $n=67$ ) were requests for information only. For the 77 calls in the latter categories the most frequent enquiries related to the toxicity and toxic profile of 1080 ( $n=13$ ), the location and timing of aerial drops ( $n=11$ ), potential for water contamination ( $n=8$ ), risks of secondary poisoning ( $n=8$ ), and risks to dogs ( $n=8$ ). Five enquiries related to availability of analytical testing. Some incidents or concerns provoked more than one enquiry. **Conclusion:** These data suggest that despite few proven human exposures to 1080, there are still public concerns over its use, particularly around inadvertent exposure via aerial drops, possible water contamination, risks of secondary poisoning via consumption of game species poisoned by 1080, and dangers to dogs (a very susceptible species). This concern was despite a favourable review by the Parliamentary Commissioner for the Environment (2011), mandatory notification of impending aerial drops, the rarity of water contamination, and the unlikelihood of human secondary poisoning.[1] This suggests that perceptions of risk from its use often exceed actual risks, requiring further public education. The dearth of occupational calls and lack of reported child ingestions was reassuring.

## Reference

- [1] Eason C. Sodium monofluoroacetate (1080) risk assessment and risk communication. *Toxicology*. 2002;181–182:523–530.

## 117. Severe toxicity with triclopyr overdose: a case report

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**Objective:** A case series of synthetic auxin-like herbicides including triclopyr suggests that their human toxicity is relatively benign [1] with only one case report describing severe toxicity with hypotension, metabolic acidosis and central nervous system depression.[2] Its pharmacokinetics in a low ingestion volunteer study report a half-life of 5.1 hours with 80% recovered unchanged in the urine.[3] We report a case of triclopyr ingestion and its treatment including dialysis. **Case report:** A 79-year-old male with a past history of hypertension and atrial fibrillation presented two hours after ingesting 250 ml of a weed killer containing 50 g/L of triclopyr (12.5 g). His Glasgow coma scale was 11 (motor 6, verbal 2, eyes 3) with heart rate 80 beats/min and blood pressure 132/87 mmHg. Respiratory rate was 19 and oxygen saturation on air 95%. A venous blood gas (VBG) taken on arrival demonstrated a severe acidaemia largely from a metabolic acidosis (pH 7.13, pCO<sub>2</sub>

58, base excess –11.0 and lactate 6.1). Subsequently his oxygen saturations fell to 84% on air and a chest X-ray demonstrated aspiration pneumonitis. Over the next three hours his condition deteriorated with an increasing oxygen requirement and a worsening metabolic and respiratory acidosis (pH 6.97, pCO<sub>2</sub> 78, base excess –16 and lactate 5.6) on VBG. He was subsequently intubated and ventilated, given 100 mmol of 8.4% sodium bicarbonate and transferred to an intensive care unit for supportive care including dialysis. Dialysis in the form of slow low-efficiency dialysis (SLED) was commenced at approximately 10 hours post-ingestion for 10 hours. Serial arterial blood gases showed an improvement in pH (7.21 to 7.41) and base excess (–12.8 to –2.1). His intensive care admission was complicated by delirium and aspiration pneumonia but he was discharged home well after a 33-day admission. Triclopyr was detected in blood using liquid chromatography mass spectrometry. **Conclusion:** Triclopyr ingestion can cause severe toxicity in deliberate ingestion and dialysis appears to have a role in its treatment, particularly in reversing the acidosis.

## References

- [1] Park JS, Seok SJ, Gil HW, et al. Clinical outcome of acute intoxication due to ingestion of auxin-like herbicides. *Clin Toxicol (Phila)*. 2011;49:815–819.
- [2] Kyong YY, Lee KU, Choi KH. Severe systemic intoxication following triclopyr-TEA ingestion. *Clin Toxicol (Phila)*. 2010;48:942–944.
- [3] Carmichael NG, Nolan RJ, Perkins JM, et al. Oral and dermal pharmacokinetics of triclopyr in human volunteers. *Hum Toxicol*. 1989; 8:431–437.

## 118. Clinical characteristics of zinc phosphide poisoning in Thailand

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**Objective:** To describe clinical characteristics and outcomes of zinc phosphide poisoning which is a common rodenticide and to evaluate whether prognosis can be determined by clinical presentation. **Methods:** We performed a retrospective study with data from the Ramathibodi Poison Center Toxic Surveillance System, during a three-year period. **Results:** There were 455 poisoning cases involving zinc phosphide. Most were male (60.5%) and from the central region (71%). The mean age was 39.9 ± 19.2 years. The most common route was oral exposure (99.3%). Most patients showed normal vital signs, oxygen saturation and consciousness at the first presentation. The three most common clinical presentations were gastrointestinal (68.8%), cardiovascular (22%) and respiratory signs and symptoms (13.8%). Most patients had normal blood chemistry laboratory results and chest X-ray findings on presentation. The median hospital stay was 2 days and the mortality rate was 7%. About 70% of patients received gastrointestinal decontamination including gastric lavage and single dose activated charcoal. Thirty-one patients were intubated and required ventilator support. Inotropic drugs were given to 4.2%. Four moribund patients also received hyperinsulinemia-euglycemia therapy and intravenous hydrocortisone, however they all died. We found that age, time to treatment, vital signs,

electrolytes and creatinine at presentation, intubation and inotropic drug therapy during the hospital stay were statistically significantly different between the patients that died and those that survived ( $p < 0.05$ ). **Conclusion:** Zinc phosphide poisoning still results in fatalities. From our study, patients presenting with shock or tachypnea or tachycardia or abnormal biochemical changes (especially acidosis) or acute kidney injury might be more at risk of severe toxicity and should be closely monitored along with aggressive treatment.

## 119. Surveillance of acute plant protection pesticide-related poisonings in Italy

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**Objective:** Regulation 2009/1185/EU on sustainable use of pesticides requires reporting from European Member States on plant protection pesticide (PPP)-related poisonings. These data can provide an informative basis to identify emerging problems, support development of preventive and regulatory measures and evaluate their impact. In Italy, surveillance of acute PPP-related poisonings (SAPReP), based on Poison Control Centre data, has been implemented since 2001 by the Italian National Institute of Health and the National Poison Control Centre in Milan. The present contribution is aimed at characterizing PPP-related poisonings identified in Italy. **Methods:** Information on cases notified to SAPReP during 2007–2012 were reviewed and classified according to standard rules: the reported exposures were grouped according to main category of use and chemical class, as indicated by Regulation (EC) No 1185/2009 concerning statistics on pesticides. Each case was reviewed to evaluate the association between exposure and clinical effects. Severity of poisonings was assessed according to Poisoning Severity Score.[1] **Results:** There were 2108 cases of accidental PPP-related poisonings over the study period. Most involved males (1442, 68%; females 442, 20%; gender unknown 224, 12%). About 50% of poisonings occurred at work, in agricultural settings, and 36% at home. Some 70% of exposures occurred between May and September. Severity of poisoning was low in 84% of cases (1774), moderate in 14% (305) and high in 1% (28). One fatal case was identified. Clinical effects most frequently reported included gastrointestinal (1316; 28%), ocular (933; 20%), dermatological (585; 13%), and respiratory (562; 12%) signs/symptoms. Insecticides/acaricides were involved in 42% of poisonings, fungicides/bactericides in 16%, herbicides in 15%, and soil sterilants in 13%. Five mass exposures were identified: two incidents were caused by off-site drift of metam sodium, a soil sterilant, and involved 86 and 103 by-standers, respectively; two incidents were caused by chlorpyrifos methyl, an organophosphate insecticide/acaricide (one occurred in a hospital, 10 cases; one occurred in agricultural setting, 20 agricultural workers); one incident was caused by phenthoate and involved 40 agricultural workers. **Conclusion:** Our findings indicate that acute pesticides-related poisonings continue to be an important health factor in Italy. Furthermore, it provides an example of how reporting PPP-related poisoning could be standardised in order to support comparability between data collected by Member States.

## Reference

- [1] Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998;36:205–213.

## 121. Death cap mass poisoning of refugees and reporting channels for acute poisoning cases

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**Objective:** Arrival of a high number of refugees from Syria, Albania and other countries during summer/autumn 2015 led to an unusual health problem in Germany when several groups of migrants collected and consumed death cap mushrooms (*Amanita phalloides*). A strong increase in case numbers of death cap poisonings has been recorded in Germany within a short period of time. Using national and European health threat reporting channels, the emerging risk was rapidly communicated. An overview of the situation regarding poisonings with death cap in refugees in Germany was obtained. **Methods:** Analysis of reports from poisons centres (PC) and hospitals, analysis of media reports and exploration of email messages exchanged between national institutions. **Results:** The Hannover Medical School published a press release on a local outbreak of death cap poisonings of refugees on 16 September 2015. The Federal Institute for Risk Assessment (BfR) received information on the first case series of poisoning by PC Göttingen on 17 September. On the same day, BfR in its capacity as a European Food Safety Authority (EFSA) Focal Point received early and urgent information regarding an outbreak of poisoning of refugees due to ingestion of death cap treated in three hospitals in northern Germany sent by the Lower Saxony Federal State Office of Health via the Robert Koch Institute. On the 18 September the information was submitted by BfR to all German PCs. On a European level, the outbreak was reported to the Rapid Alert System for Food and Feed (RASFF) and to the Early Warning Response System (EWRS), the EU institution responsible for acute, cross-border health threats (Decision No 1082/2013/EU). BfR started a survey involving PCs and hospitals mentioned in media reports. At least 40 cases were registered in August and September 2015, including at least six cases with liver transplantations and three lethal outcomes. Only three death cap poisonings of refugees were notified after September 2015. Whether an early widespread distribution of information on the event (a poster had been designed, translated into eight languages and successfully distributed by Hannover Medical School via their refugee aid network) or changing weather conditions has led to a termination of the outbreak remains unclear. **Conclusion:** This acute poisoning outbreak has demonstrated the importance of networking among authorities, institutions and facilities. Many parties involved were successful in rapidly exchanging important information. Early risk communication, in particular early risk identification and assessment enabled adequate action at all levels throughout Germany.

## 122. Clinical outcomes and predictive factors in “massive” paracetamol overdose

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**Objective:** There is currently debate as to whether standard acetylcysteine regimens are adequate for “massive” paracetamol overdoses.[1] This study evaluated determinants of outcome in “massive” paracetamol overdose. **Methods:** Retrospective analysis of data prospectively collected on a purpose-designed clinical toxicology database on presentations to two UK teaching hospitals 2005–2013. Patients with single acute overdoses were included if they had ingested >30 g or an initial plasma paracetamol concentration >2-fold the 150 mg/L paracetamol nomogram treatment line. Paracetamol dose, time to presentation/acetylcysteine administration, and ratio of measured plasma paracetamol concentration (APAP<sub>pl</sub>) to the 150 mg/L treatment line at the corresponding time (APAP<sub>t</sub>) were compared to peak International Normalized Ratio (INR) and ALT/AST. **Results:** Of 127 cases identified 88 (69.2%) were female and median (IQR) age was 32 (23–42) years. Ingested dose was known in 91.3% (116), with median (IQR) of 24 g (16–36 g). Time to presentation was 5.5 h (3.5–13.3 h); 53 (41.7%) presented >8 h post-ingestion. Time to acetylcysteine was known in 78 (61.4%). Median (IQR) APAP<sub>pl</sub>:APAP<sub>t</sub> was 182 mg/L (79–256); 28 (22.0%) patients had a rise in ALT/AST >5-fold the upper limit of normal (ULN), of whom 17 (13.4%) > 1000 IU/L and 4 (3.1%) > 10,000. INR was >2 in 12 (9.4%) patients, and >6.5 in 2 (1.6%) cases. There were significant correlations between serum ALT/AST and time to presentation ( $r=0.21$ ,  $p=0.02$ ) and to acetylcysteine ( $r=.30$ ,  $p=0.008$ ); and INR and time to acetylcysteine ( $r=0.27$ ,  $p=0.02$ ). Overall, higher APAP<sub>pl</sub>:APAP<sub>t</sub> were associated with greater peak ALT/AST and INR ( $r=0.33$ ,  $p=0.0002$ ). There was no correlation between reported dose nor unadjusted APAP<sub>pl</sub>:APAP<sub>t</sub> and either ALT/AST or INR. Patients who presented >10 h post-overdose had higher APAP<sub>pl</sub>:APAP<sub>t</sub> ( $p=0.001$ ) and increased risk of ALT/AST >5x ULN ( $p=0.02$ ). Of the 29 (37.1%) receiving acetylcysteine within 8 h, 2 (7%) developed INR >2 and 4 (17.2%) had AST/ALT >5x ULN (of whom 2 had AST/ALT >1000IU/L). Liver injury was predicted by a high APAP<sub>pl</sub>:APAP<sub>t</sub> ( $p=0.03$ ). Amongst patients receiving acetylcysteine >8 h, 10 (20.4%) developed an INR >2 and 17 (34.7%) AST/ALT >5-fold ULN. Mean APAP<sub>pl</sub>:APAP<sub>t</sub> was similar between liver injury patients who received acetylcysteine before compared to after 8 h. **Conclusion:** “Massive” paracetamol overdose is associated with high rates of liver injury despite treatment, particularly in patients presenting late; even in those presenting at <8 hours a significant minority develop liver injury. High APAP<sub>pl</sub>:APAP<sub>t</sub> is a key predictor of injury, rather than reported dose ingested or absolute plasma paracetamol concentration.

### Reference

- [1] Chiew AL, Isbister GK, Duffull SB, et al. Evidence for the changing regimens of acetylcysteine. *Br J Clin Pharmacol.* 2016;81:471–481

## 123. Pharmacokinetic modelling of a high dose acetylcysteine regimen based on the SNAP trial

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**Objective:** A novel acetylcysteine (“SNAP”) regimen (100 mg/kg over 2 hours then 200 mg/kg over 10 hours) causes fewer adverse reactions [1] and is likely to be effective in most patients, but more prolonged therapy may be needed in those with substantial overdose. This can be achieved by administration of a further 200 mg/kg infusion over 10 hours (extended SNAP regimen). We aimed to compare predicted plasma acetylcysteine concentrations of two extended 22 hour SNAP regimens (with and without a 2 hour break between the first and second 10 hours infusions) with the current UK acetylcysteine regimen (150 mg/kg over 1 hour, 50 mg/kg over 4 hours then 100 mg/kg over 16 hours). **Methods:** Pharmacokinetic modelling using a 3-compartmental model was performed using published pharmacokinetic parameters following an intravenous bolus of acetylcysteine [2] comparing the two extended SNAP regimens with the current standard acetylcysteine regimen. **Results:** Mean simulated peak plasma acetylcysteine concentration with the current regimen was 568 mg/L at 1 hour compared to 222 mg/L at 2 hours with the extended SNAP regimens. After peaking, the mean simulated plasma acetylcysteine concentration declined slowly to around 120 mg/L at the end of the extended SNAP regimen but declined rapidly to a concentration below that of the SNAP regimen within 1.5 hours with the current regimen. Following discontinuation of the 12 hour SNAP regimen, plasma concentrations rapidly declined to the level achieved using the current regimen within 2 hours but rapidly increased within 1.5 hours to around 200 mg/L when a second 200 mg/kg 10-hourly bag is started after 2 hours. **Conclusion:** The pharmacokinetic model suggests that a further 10-hour 200 mg/kg infusion at the end of the 12 hour infusion (total 500 mg/kg over 22 hours), provides plasma acetylcysteine concentrations of 120–220 mg/L, which are unlikely to cause delayed adverse reactions. Further studies are needed to determine the efficacy of this regimen for patients with massive paracetamol overdoses or early hepatotoxicity.

### References

- [1] Bateman DN, Dear JW, Thanacoody HKR, et al. Reduction of adverse effects from intravenous acetylcysteine treatment for paracetamol poisoning: a randomized controlled trial. *Lancet.* 2014;383:697–704.
- [2] Brown M, Bjorksten A, Medved I, et al. Pharmacokinetics of intravenous N-acetylcysteine in men at rest and during exercise. *Eur J Clin Pharmacol.* 2004;60:717–723.

## 124. The standard treatment protocol is inadequate following overdose of extended release paracetamol: a pharmacokinetic and clinical analysis of 53 cases

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**Objective:** Experience shows that treatment of overdose with extended release (ER) paracetamol formulations poses challenges beyond those encountered with immediate release (IR) preparations. This may be linked to differences in the exposure profile between the products. The aim of the study was to describe the pharmacokinetics of paracetamol following acute overdoses of an ER formulation (Alvedon 665<sup>®</sup>), containing 2/3 of extended release, 1/3 immediate release, and assess whether present treatment recommendations are adequate. **Methods:** Hospital case reports including laboratory values concerning acute intake of ER paracetamol in toxic doses ( $\geq 10$  g or 140 mg/kg) were collected retrospectively between 2009 and 2015. Inclusion criteria were a reported dose, estimated time of intake and determined serum concentrations. Graphical analysis and descriptive statistics (R 3.1.3 and Excel) as well as population pharmacokinetic modeling (NONMEM 7) were used to describe the observed data. **Results:** In total 53 cases were identified. The mean age was 30.5 years (range 13–68), median reported dose 23 g (range 10–166) and 76% were females. The number of serum paracetamol concentrations per individual ranged from 1 to 10. Forty-three patients were treated with N-acetylcysteine (NAC). Liver impairment occurred in 21%. The pharmacokinetic analysis showed saturable absorption as the duration of the absorption was correlated to increasing amounts of ingested drug. A plateau with high serum concentrations for 24 hours or more were observed in 21%, and 5 patients had a second peak approximately 12 hours (range 8–19) after intake. Late crossing of the standard treatment nomogram (Campbell line) were seen in 19% of the cases. Seven patients developed liver impairment despite timely treatment with NAC, the majority with high serum concentration for a prolonged time. **Conclusion:** Treatment recommendations based on IR formulations are inadequate after intake of toxic doses of this ER preparation. Risk assessment using initial serum samples 4–8 hours after estimated intake cannot be trusted. Serial paracetamol measurements, initially and up to at least 18 hours after intake, are essential to determine if NAC is required and to what extent. As liver impairment developed in patients treated with the currently recommended NAC regime, we suggest that a higher maintenance dose of NAC should be given in cases with persistently high concentrations of paracetamol. Treatment should be continued beyond 20 hours in patients with detectable concentrations and/or sign of significant liver impairment. Further studies are required to better determine the optimal management for this ER formulation.

## 125. Citalopram overdose in children and adolescents

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**Objective:** Information on the toxicity of citalopram in paediatric patients is limited, especially in children  $>6$  years. Furthermore, studies are needed to reconfirm the suggested triage guideline for the treatment of children  $<6$  years as safe and reliable.[1] The aim of this study is to provide more data on this topic. **Methods:** A multicentre retrospective analysis of acute overdoses of citalopram in children and adolescents. Inclusion criteria were single substance ingestion, defined dose, and documented follow up for at least 10 hours. Severity of symptoms was assessed according to the Poisoning Severity Score. **Results:** A total of 109 cases met the inclusion criteria. Patients involved were 51 babies/toddlers (0.08–5 years), 18 schoolchildren (6–13 years), and 40 adolescents (14–17 years). Doses ranged between 5–100 mg (0.4–6.7 mg/kg) in babies/toddlers, 10–1600 mg (0.5–22.7 mg/kg) in schoolchildren, and 60–1600 mg in adolescents. Overall 36.7% of patients remained asymptomatic. More than half the children and adolescents (52.3%) developed only mild symptoms. The lowest dose causing mild symptoms was 10 mg (0.67 mg/kg), 20 mg (0.49 mg/kg), and 60 mg in babies/toddlers, schoolchildren and adolescents, respectively. In children  $<6$  years no moderate toxicity was observed. However, a 13-year-old child and 11 adolescents suffered from moderate symptoms after ingestion of 260 mg (3.3 mg/kg) and 100–1600 mg, respectively. Otherwise, adolescents tolerated up to 400 mg without any toxicity. The clinical feature of poisoning is particularly characterised by neurologic symptoms like fatigue (17.4%), dizziness (17.4%), tremor (11.6%), somnolence (8.7%), tachycardia (18.8%), and nausea/vomiting (33.3%). Infrequently, QT prolongation (5.8%) was observed. Seizures (11.6%) only developed in adolescents at doses from 400 mg. **Conclusion:** Most cases of citalopram overdose in this study resulted in no or only mild effects (89%). Severe symptoms were not observed. There is no correlation between dose and severity of symptoms. Results of the present study confirm the assumption that citalopram  $<5$  mg/kg is not likely to cause serious toxicity in children  $<6$  years.[1] Nevertheless, further investigations are necessary to assess the toxicity of citalopram especially in children  $>6$  years.

### Reference

- [1] Herrington L, Miller JL, Geller RJ, et al. Pediatric ingestion of citalopram: What is a safe dose for home management? Clin Toxicol (Phila). 2015;53:723–724.

## 126. Examining methotrexate exposures reported to the UK National Poisons Information Service 2004–2015: highlighting adverse reactions and avoidable therapeutic errors

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**Objective:** To investigate the circumstances surrounding methotrexate overdose reported to the UK National Poisons Information Service (NPIS). **Methods:** Using data extracted from UK Poisons Information Database (UKPID), a centralised NPIS telephone enquiry database, we reviewed the number and nature of incidents involving methotrexate from 1 April 2004 to 31 March 2015. **Results:** Of 1469 enquiries the most common cause of exposure was therapeutic error ( $n=770$ , 52.4%), compared to 17% of total NPIS enquiries related to therapeutic error. Other circumstances were accidental ( $n=340$ , 23.1%), intentional ( $n=261$ , 17.8%) and adverse reactions ( $n=33$ , 2.2%). Most exposures occurred at home ( $n=1333$ , 90.7%); 513 (34.9%) patients were male. Of the 1285 enquiries where poisoning severity score (PSS) was reported 948 (73.8%) were asymptomatic. Minor symptoms were reported in 8.1% of accidental exposures, 10.8% of therapeutic errors, 25.8% of intentional exposures and 14.3% of adverse reactions. Moderate and severe symptoms ( $n=82$ ) were reported in 2% of accidental exposures, 3% of therapeutic errors, 8% of intentional exposures and 75% of adverse reactions. Of the adverse reactions 11 (33%) developed in hospital; 51.5% were male. Symptoms included pancytopenia ( $n=8$ ), abnormal hepatic function ( $n=8$ ), acute renal failure ( $n=7$ ), abnormal renal function ( $n=4$ ), anaemia ( $n=4$ ), granulocytopenia ( $n=3$ ), diarrhoea ( $n=3$ ), ulceration ( $n=3$ ) and thrombocytopenia ( $n=3$ ). The mean dose was 30 mg (1–300 mg) for accidental exposures, 82.9 mg (2.5–9800 mg) in therapeutic errors, 105.6 mg (5–2800 mg) in intentional exposures and 2860 mg (10–25000 mg) in adverse reactions. Of the 770 therapeutic errors 416 (54%) were acute on therapeutic, 64 (8.3%) staggered, 112 (14.5%) sub-acute and 21 (2.7%) chronic. Most intentional overdoses ( $n=96$ , 36.8%) took place on a background of therapeutic use. Of 1110 accidental or therapeutic error exposures methotrexate was mistaken for folic acid ( $n=28$ , 2.5%), prednisolone ( $n=4$ ) or another medication ( $n=5$ ). The 10 mg tablets were mistaken for 2.5 mg tablets in 53 (4.8%) cases. In 275 (24.8%) cases, patients took a repeat of their once weekly dose. Actions were required in 60.6% ( $n=890$ ). Actions recommended were investigations ( $n=428$ , 29.1%), supportive care ( $n=228$ , 15.5%), antidote ( $n=186$ , 12.6%), monitoring vital signs ( $n=65$ ), referral to hospital ( $n=19$ ), referral to general practitioner ( $n=8$ ), cardiac monitoring ( $n=6$ ) and haemodialysis ( $n=3$ ). **Conclusion:** Enquiries about methotrexate more frequently involve therapeutic errors than overall NPIS enquiries (52.4% versus 17%). Therapeutic errors commonly involve acute on therapeutic ingestions (54%), producing no symptoms (83.2%). Potentially avoidable errors included repeating once weekly doses (24.8%) and tablet identification errors (8.1%).

## 127. Calcium channel blocker poisonings in Denmark: 5 years' data from the Danish Poison Information Center

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**Objective:** Poisoning with a calcium channel blocker (CCB) is a serious medical event that often requires treatment in a hospital and can be fatal. The objective of this study was to describe the population poisoned with CCBs and the frequency and consequences of CCB poisonings in Denmark during the past 5 years. **Methods:** All enquiries concerning CCBs reported to the Danish Poison Information Center (DPIC) from January 2009 to February 2015 were paired with outcome data from the Danish National Patient Register and analysed retrospectively. **Results:** Of a total of 126,987 enquiries, 350 (0.3%) concerned CCBs. When divided in age decades, children from zero to ten years of age were the most frequently represented (22%) followed by the age groups: 41–50 (15%), 51–60 (14%), 61–70 (14%) and 71–80 (12%) years. The age groups: 11–40 and >80 years were least exposed (24% in total). Amlodipine was involved in 58% of all cases. Enquiries concerning females (56%) were more frequent than males (44%), but there were no gender differences in the proportion of intentional compared to accidental poisonings (the latter comprised 43% of cases). Of all enquiries, 24% involved children (<16 years), and these were almost exclusively due to accidental poisonings (93%). The severity of the poisoning (by risk assessment of DPIC) were most often moderate (52%) and severe (27%). Most of the patients required hospitalisation (79%) including all children. Unintentional poisonings most commonly involved only one drug (78%), whereas most intentional poisonings involved multiple drugs (84%). Patients with psychiatric diagnoses were more frequently involved in intentional ingestion (70%) than patients without psychiatric diagnosis (57%). In total, seven patients (2%) died; all were intentional exposures. All but one of the fatal poisonings died within the first two days of hospital admission. The CCBs involved in multidrug fatal poisoning were amlodipine ( $n=3$ ), verapamil ( $n=1$ ), and felodipine ( $n=1$ ). Verapamil was the only cause of fatal CCB single-drug poisonings ( $n=2$ ). **Conclusion:** From 2009 to 2015, enquiries to the DPIC concerning CCBs were infrequent, but a quarter involved children and most cases resulted in hospitalisation. Mortality occurred only in adults with intentional exposures, and only verapamil led to death in single-drug poisoning.

## 128. Severe hypercalcemia secondary to chronic vitamin D overdose in an infant

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**Objective:** The American Academy of Pediatrics recommends 400 IU of vitamin D supplement per day for children <1 year. We report a case of accidental vitamin D overdose resulting from parental confusion over concentration differences in two different brands of supplement. **Case report:** A full-term, breast-fed infant born while on vacation in Canada was recommended to start one dropper full (20 mL) of an unknown Canadian brand vitamin D supplement. Two months later, the family returned to the US where they purchased a new bottle of vitamin D drops unaware of a difference in concentration. The mother continued to administer an entire dropper full of drops instead of the recommended one drop intermittently over the next eight months. The mother brought the patient to the ED at 10 months of age for progressively worsening lethargy, emesis, poor weight gain, and failure to

meet developmental milestones. In the ED, the patient was somnolent but rousable. Her physical examination was remarkable for an inability to roll, crawl or pull to stand. Her initial vital signs were blood pressure 101/45 mmHg, heart rate 138, temperature 37°C, respiratory rate 24/min, oxygen saturations 97% on room air and weight 7.3 kg (7th percentile). Laboratory results were significant for serum calcium 16 mg/dL, ionized calcium 2.01 mmol/L, phosphorus 3.3 mg/dL, intact parathyroid hormone 5.6 pg/mL, parathyroid hormone-related protein (PTHrP) 9.5 pmol/L (ARUP labs), 1,25-vitamin D 339 pg/mL, 25-vitamin D >300 ng/mL, and leukocytosis (17.4 mCL). Ultrasound of the kidney showed bilateral diffusely increased echogenicity of renal medulla consistent with nephrocalcinosis. Electrocardiogram (EKG) did not show shortened QT or J waves. She was admitted and treated with aggressive intravenous fluid hydration, furosemide, and calcitonin. She remained hypercalcemic throughout her hospital stay and was discharged on hospital day 13 with a serum calcium of 11.3 mg/dL. One month after discharge serum calcium was 10.8 mg/dL and 25-OH-vitamin D 87 ng/mL. **Conclusion:** Chronic overdose of vitamin D can result in serious toxicity including hypercalcemia, cardiac arrhythmias, and renal dysfunction. We present a case of inadvertent vitamin D overdose secondary to differences in supplement concentrations. As public use of supplements and herbal remedies continues to increase and remains largely unregulated, physicians must be diligent about dosing instructions and patient education regarding their risks.

## 129. Salicylate poisoning: risk factors for severe outcome

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**Objective:** Acetylsalicylic acid (ASA; aspirin) poisoning remains a significant public health threat with upwards of 20,000 exposures annually in the US and morbidity/mortality rates of up to 25%.<sup>[1]</sup> Identifying predictors of severe outcome facilitates targeted treatment to lower these rates. In this study, we aimed to establish early predictors of severe in-hospital outcomes in Emergency Department (ED) patients presenting with ASA poisoning. **Methods:** This was a secondary data analysis of ASA overdoses from a prospective cohort study of suspected acute drug overdoses at two urban university teaching hospitals from 2009–2013. Patients were enrolled consecutively and were considered eligible for inclusion based on clinical suspicion of ASA ingestion. Children (<18 years) and alternate diagnoses were excluded. Demographics, clinical parameters, serum ASA concentrations, treatment modalities and death/admission rates were collected from the medical record. Severe outcome was defined as a composite occurrence of any of the following: acidemia (pH <7.3 or bicarbonate <16 mEq/L), hemodialysis, or death. **Results:** In total 48 patients met inclusion criteria, with 43.8% male, median age 32 years, mean initial ASA concentration 28.1 mg/dL, and 10 (21%) were classified as severe outcome. There were two deaths, neither of whom received hemodialysis. Patients were treated with sodium bicarbonate in one-third of cases, while 54.2% received activated charcoal and 64.6% were admitted. Univariate analysis indicated that age ( $p=0.04$ ,  $t$ -test), respiratory rate (RR) ( $p=0.04$ ,  $t$ -test), creatinine ( $p=0.05$ ,  $t$ -test), lactate ( $p=0.002$ ,  $t$ -test), coma ( $p=0.05$ , chi-square), and presence of co-ingestants ( $p=0.04$ , chi-square) were significantly associated with severe outcome, while ASA alone had no association. However, when adjusted for serum ASA concentration, only age (OR 1.02 per additional year, CI 1.0–1.1), RR (1.09 per additional breath/min,

CI 1.03–1.15), creatinine (2.8 per additional mg/dL CI 1.1–7.1), and co-ingestants (OR 6.4, CI 2.3–17.8) were independent predictors of severe outcome. **Conclusion:** We have derived independent predictors of severe outcome from acute ASA poisoning, which can aid in identifying patients who require aggressive treatment. Age, RR, creatinine, and co-ingestants are predictive of severe outcome in ED patients with acute ASA poisoning, while serum ASA concentration alone is not. Despite the severity of these cases, only one-third received sodium bicarbonate, suggesting potential barriers to administration which require further study.

## Reference

- [1] Kreplick LW. Toxicity, salicylate. *eMedicine J.* 2001;2:6.

## 130. Accidental epidural or intrathecal administration of thiocolchicoside can be lethal

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**Objective:** Thiocolchicoside, a glycosulfurate analogue of colchicine, is a muscle relaxant (claimed to possess GABA-mimetic and glycinergic actions) promoted in some EU and South America countries, and in Mexico, as symptomatic treatment of painful muscle spasm, especially if associated with acute lower back pain. After intramuscular administration, minimal adverse effects (gastrointestinal discomfort, hypotension, agitation) have been reported occasionally. No data are available in the medical literature about erroneous intrathecal administration and consequent adverse effects. We report seven cases of erroneous epidural/intrathecal administration of thiocolchicoside. **Case series:** In a 20-year period 7 patients were identified and studied (42–65 years; M/F 5/2). In all cases, except one (in which erroneous self-administration in an epidural catheter occurred) thiocolchicoside (1 vial; 4 mg/2 ml) was erroneously given by epidural or intrathecal injection during an outpatient lumbar infiltration procedure. Local anesthetics (lidocaine/xylocaine/bupivacaine) associated with ketoprofen or corticosteroids (triamcinolone/methylprednisolone) were co-administered. Severe lumbar pain ( $n=5$ ) associated with perineal or saddle paresthesia or anesthesia ( $n=3$ ) appeared within 30 minutes. Clinical manifestations worsened during the following 2 hours in all cases, with repeated and unresponsive tonic-clonic seizures (100%), coma (86%), persistent lumbar/pelvic pain (86%), rectal tenesmus (57%), repeated spontaneous ejaculation (40%), hyperthermia and severe hypertension (57%). Brain computerised tomography (CT) scan evidenced air microembolism in one case. Four patients died (50% within 10 hours), and in two of them thiocolchicoside was detected in cerebrospinal fluid. **Conclusion:** Intrathecal administration of a xenobiotic may be related with potentially lethal adverse effects, and it can occur from preparation/dosing error or inadvertent penetration in the dura. Inadvertent and erroneous administration via pump delivery systems results in massive overdose. Some factors influence the chemical toxic effects (e.g. dosage, osmolality, lipophilicity, baricity).<sup>[1]</sup> Some drugs (local anesthetics, corticosteroids) are usually given by epidural/intrathecal in anesthesia/analgesia procedures. Conversely, thiocolchicoside epidural/intrathecal injection causes severe neurotoxic effects (autonomic instability, pain, pelvic



anesthesia, seizures and coma) with rapid lethal outcome in 60% of our cases. No particular predictive factors for fatal evolution have been identified. Considering the potential and unpredictable dramatic effects, these cases should be treated immediately in high intensity care units, and recovery from cerebrospinal fluid drainage should be evaluated. Outpatient lumbar infiltration should be considered a high risk procedure.

## Reference

- [1] Rama BR. Intrathecal administration of xenobiotic. In: Hoffman RS, Howland MA, Lewin NA, et al, eds. *Goldfrank's Toxicologic Emergencies*. 10th ed. New York, USA: McGraw-Hill Education, 2015:703–710.

## 131. Co-administration of methadone and ondansetron associated with torsades de pointes

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**Objective:** To describe two patients treated with methadone and ondansetron who developed QT prolongation leading to torsades de pointes (TdP). **Case report:** Case 1: A 55-year-old man with a past medical history of hypertension and heroin abuse presented to the emergency department (ED) in police custody with a chief complaint of "I am in withdrawal". The patient had last used heroin several hours prior to presentation. He denied chest pain. Initial vital signs were: pulse 49 beats/min, blood pressure 224/113 mmHg, respiratory rate 16/min and oxygen saturations normal. Electrocardiogram (ECG) showed sinus bradycardia, QT 476 ms, rate of 52 beats/min, small ST elevations in V1–V3, and T wave inversions in leads I, V5, and V6. Serum potassium was 3.5 mmol/L. Hypertension and ECG changes prompted admission. Nine hours later, he received ondansetron 4 mg IV to treat nausea and vomiting, and methadone 10 mg IM to treat opioid withdrawal. Two hours later he received an additional dose of ondansetron 4 mg IV and 30 minutes later he became pulseless, with TdP on the monitor. The patient returned to sinus rhythm following defibrillation. ECG after defibrillation showed QT 640 ms with a rate of 53 beats/min. Case 2: A 58-year-old man with a past medical history of polysubstance abuse on methadone presented to the ED with nausea and vomiting. He last took methadone 80 mg by mouth the night prior to arrival and had used heroin and smoked a synthetic cannabinoid receptor agonist two hours prior to arrival. Initial vital signs were: pulse 47 beats/min, blood pressure 144/69 mmHg, respiratory rate 14/min and oxygen saturations 99%. The initial potassium was 4.3 mmol/L with moderate hemolysis. The patient received ondansetron 4 mg IV one hour after arrival. Thirty minutes later, the patient became diaphoretic and ill-appearing. An ECG demonstrated a QT 528 ms and heart rate 54 beats/min. A repeat ECG 10 minutes later showed QT 596 ms and heart rate 52 beats/min. Repeat potassium was 3.5 mmol/L. The patient was admitted to the coronary care unit, where he had multiple episodes of TdP requiring defibrillation. **Conclusion:** Methadone is commonly used to treat opioid dependence and withdrawal. Patients on methadone may receive ondansetron to treat nausea and emesis. Both medications

prolong the QT interval, and methadone contributes to bradycardia, increasing the risk for TdP. When administering QT-prolonging medications, providers should be aware of additional risk factors for developing TdP, such as bradycardia and hypokalemia.

## 132. Precipitated opioid withdrawal from naltrexone injection

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**Objective:** To describe the clinical effects and management of severe precipitated opioid withdrawal (POW) after injection of intramuscular naltrexone (Vivitrol). **Case report:** A 25-year-old male with a history of polysubstance abuse presented to the Emergency Department (ED) with agitation and altered mental status. A few hours earlier he had received extended release intramuscular naltrexone (ERIN) 380 mg intramuscularly at the conclusion of a 12-day detoxification program for heroin. The patient reported to the ED provider surreptitious heroin use multiple times during the detoxification period including 2–3 bags of heroin on the day prior to the naltrexone injection. The patient reported the onset of withdrawal shortly after the naltrexone injection and denied receipt of a preceding test dose of opioid antagonist. In the ED his vital signs were blood pressure 139/72 mmHg, heart rate 111/min, respiratory rate 22/min, temperature afebrile and oxygen saturation 96% on room air. An electrocardiogram showed sinus tachycardia. The physical examination was notable for bilaterally dilated reactive pupils, diaphoresis, agitation and delirium. The patient received lorazepam 6 mg, midazolam 2 mg, and haloperidol 10 mg without effect. He was intubated and placed on propofol, lorazepam and dexmedetomidine infusions. The following day the patient was extubated and weaned from sedation. On day three of hospitalization he was oriented to person and year, and the vital signs were normal. By the next day his mental status improved to baseline and he elected to leave against medical advice. **Conclusion:** IM extended release naltrexone is an approved therapy to prevent relapse of opioid and alcohol abuse. POW after ERIN can be life-threatening though relatively short-lived compared to the duration of action of the drug. Documented POW after ERIN is limited to one case report. In that case a 17-year-old opioid-dependent girl had POW soon after receiving her third dose of ERIN in the setting of continued oxycodone use throughout antagonist therapy.[1] To our knowledge this is the first reported case of iatrogenic POW induced by ERIN after recent heroin use. Our patient recovered fully after 3 days, which is consistent with the course of resolution of opioid withdrawal and much more rapid than the fall in naltrexone concentrations. Adequate detoxification and antagonist testing should be accomplished prior to initiation of ERIN therapy.

## Reference

- [1] Fishman M. Precipitated withdrawal during maintenance opioid blockade with extended release naltrexone. *Addiction*. 2008;103:1399–1401.

## 134. Comparison of atypical antipsychotic exposures in young children reported to US poison centers

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**Objective:** With increasing use of atypical antipsychotics there has been an increase in the number of exposures reported to poison centers. Previous reports are limited to small case series, data from one poison center and/or encompass relatively short time periods. The objectives of this study were to evaluate national poison center data involving atypical antipsychotic exposures in young children and to compare outcomes amongst selected atypical antipsychotic agents. **Methods:** A retrospective study of US National Poison Data System from 2005–2013 of single substance exposures to five atypical antipsychotics in children <6 years of age and followed to known outcome was performed. Data were evaluated for circumstance, clinical effects, management sites and outcomes. **Results:** There were 16,935 cases that met the inclusion criteria: 5018 aripiprazole, 1735 olanzapine, 3904 quetiapine, 4778 risperidone and 1500 ziprasidone. The majority of exposures were unintentional general (i.e. exploratory in nature) (90.6%). Therapeutic error occurred more often with risperidone (19.9%) than with the other four drugs (2.7%). Most frequently reported clinical effects were drowsiness/lethargy (35.6%), tachycardia (6.9%), agitation (4.0%), ataxia (3.3%), vomiting (3.0%) and dystonia (2.2%). Clinical effects occurred in 29.3% of quetiapine, 40.1% of risperidone, 56.6% of ziprasidone, 57.9% of olanzapine and 59.5% of aripiprazole. Drowsiness/lethargy occurred most often with aripiprazole (47.6%), ziprasidone (46.5%) and olanzapine (45.1%) and less commonly with quetiapine (20.5%) and risperidone (28.6%). Olanzapine had the highest frequency of agitation (12.6%). Tachycardia occurred most often with olanzapine (11.4%) and least often with quetiapine (4.4%). Management sites were non-healthcare facility (28.0%), treated/discharged from emergency department (48.9%), admitted to noncritical care (11.4%), admitted to critical care (9.5%) and other/unknown (2.2%). Admission was least likely for risperidone (14.0%) and quetiapine (12.0%) and most likely for olanzapine (33.0%). Coded outcomes were no effect (53.3%), minor effect (33.7%), moderate (12.1%) and major (0.9%). More serious toxicity (moderate/major) occurred most often with aripiprazole (16.5%), olanzapine (19.1%) and ziprasidone (20.6%) and least often with quetiapine (5.4%) and risperidone (10.9%). **Conclusion:** Overall outcomes were good, with major toxicity in less than 1% of cases. Risperidone and quetiapine exposures resulted in less toxicity than the other atypical antipsychotics. Possible reasons for these findings include higher frequency of therapeutic errors which usually involve lower doses with risperidone and possibly lower inherent toxicity with quetiapine. Further study is warranted to confirm these findings.

## 135. Torsades de pointes due to co-administration of methadone and moxifloxacin

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**Objective:** Combinations of drugs that block hERG channels prolong the QT interval and increase the risk of life-threatening ventricular tachyarrhythmias. This is a predictable and preventable adverse reaction. Methadone is a chiral drug; levomethadone produces the opioid effect and dextromethadone is a more potent blocker of the hERG-channel.[1,2] Methadone metabolism is mediated mainly by the cytochrome P450 enzymes CYP3A4 and CYP2B6, whereby dextromethadone is metabolized mostly by CYP2B6. About 7% of Caucasians are CYP2B6 slow metabolizers resulting in a higher risk for drug-induced QT prolongation.[1] Here we explore the clinical context of an important adverse drug effect of methadone and moxifloxacin. **Case report:** A 55-year-old man with methadone substitution (220 mg/day) presented with fever (39.4 °C) and cough. The medical history included hepatitis C and HIV infection, currently without treatment. The electrocardiogram (ECG) showed sinus bradycardia (47 bpm) with a QTc interval of 460 ms (normal value <450 ms). The patient was treated with moxifloxacin 400 mg/day for suspected pneumonia. The following day the patient collapsed and a polymorphic ventricular tachycardia (torsades de pointes, TdP) was noted. Methadone and moxifloxacin were identified as potential causes and he was switched to levomethadone (at half the methadone dose) and amoxicillin/clavulanic acid. No further arrhythmias occurred and 4 days later the QTc interval was normal (420 ms). Genotyping showed the patient was not a CYP2B6 slow metabolizer. **Conclusion:** In this case, the QT prolongation and TdP could have been avoided by using another antibiotic and/or levomethadone instead of methadone. A clinical trial showed that switching methadone to levomethadone resulted in a significant QTc reduction.[2] A search of the WHO Global Database of Safety Reports revealed 263 cases of TdP associated with methadone (2000–2015), 17 with morphine (1997–2015) and 3 with levomethadone (2010–2015). Of note, the number of prescriptions was not considered. Drugs that cause QT prolongation should be used with caution and combinations of such drugs should be avoided. Alerts should be included in electronic prescription systems. Use of levomethadone instead of methadone likely reduces the risk of QT prolongation in particular in patients receiving high dose methadone.

## References

- [1] Eap CB, Crettol S, Rougier JS, et al. Stereoselective block of hERG channel by (S)-methadone and QT interval prolongation in CYP2B6 slow metabolizers. *Clin Pharmacol Ther.* 2007;81:719–728.
- [2] Ansermot N, Albayrak O, Schläpfer J, et al. Substitution of (R,S)-methadone by (R)-methadone: impact on QTc interval. *Arch Intern Med.* 2010;170:529–536.

## 136. Methadone-induced hypoglycemia in an 11-month-old child

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**Objective:** Unintentional methadone exposures can result in central nervous system (CNS) and respiratory depression. Metabolic derangements have also been reported. We report a case of an infant male who developed hypoglycemia after methadone exposure. **Case report:** An otherwise healthy 11-month-old child presented in respiratory failure. Initial glucose was 160 mg/dL. He was intubated and transferred to a large, tertiary children's hospital. Upon arrival, he was hypotensive and received dopamine and epinephrine. Laboratory evaluation was notable for a glucose of 17 mg/dL. He was given a 4 mL/kg dextrose 10% in water bolus with a subsequent glucose of 53 mg/dL. Physical exam was notable for 4 mm pupils that became pin-point and he received IV naloxone (0.1 mg/kg<sup>2</sup>) with delayed improvement in miosis and hemodynamics. The parents had a history of IV opioid abuse and were on methadone maintenance therapy. A quantitative methadone concentration was 123 ng/mL. Endocrinologic evaluation showed an elevated insulin concentration and a low serum beta-hydroxybutyric acid concentration. Metabolic evaluation, including plasma amino acids and urine organic acids, was negative. Toxicologic testing for sulfonyleureas was negative. He was extubated on hospital day 6 and was transferred to the Neurology service on hospital day 9. Methadone-induced hypoglycemia has been reported with therapeutic use in cancer patients,<sup>[1,2]</sup> and recent research has shown an association between opioids and hypoglycaemia.<sup>[3]</sup> We observed hypoketotic, hyperinsulinemic hypoglycemia after methadone exposure. Alternative explanations for hypoglycemia, namely sulfonyleurea exposure, fatty oxidation disorders, and hyperinsulinism, were negative. A proposed mechanism of opioid-induced insulin secretion is suspected. **Conclusion:** Methadone is a synthetic opioid that is used in the treatment of pain as well as opioid dependence. Pediatric patients are especially vulnerable to serious adverse outcomes with unintentional exposure, including hypoglycemia. Methadone exposure should be in the differential of hypoglycemia in the poisoned patient.

## References

- [1] Flory JH, Wiesenthal AC, Thaler HT, et al. Methadone use and the risk of hypoglycemia for inpatients with cancer pain. *J Pain Symptom Manage.* 2015;51:79–87.
- [2] Gjedsted J, Dall R. Severe hypoglycemia during methadone escalation in an 8-year-old child. *Acta Anaesthesiol Scand.* 2015;59:1394–1396.
- [3] Fournier J-P, Azoulay L, Yin H, et al. Tramadol use and the risk of hospitalization for hypoglycemia in patients with noncancer pain. *JAMA Intern Med.* 2015;175:186–193.

## 137. Massive paracetamol overdose: an observational study

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**Objective:** Describe clinical characteristics and outcomes of “massive” paracetamol overdose. **Methods:** Observational study, over varying time periods from two toxicology units (5 and 20 years) and calls to NSW (3 years) and Queensland (1 year) Poisons Information Centre (PIC). Included were acute ingestions of immediate-release paracetamol  $\geq 40$  g, ingested over  $< 8$  h. Toxicology unit data was extracted from clinical databases and medical records. Clinical data from PIC cases was collected prospectively as part of the Australian Paracetamol Project. To compare paracetamol concentrations, the ratio of the first paracetamol concentration taken  $> 4$  to  $< 15$  h post-ingestion to the standard (150 mg/L at 4 h) nomogram line, at that time point was calculated. **Results:** Overall 145 paracetamol overdoses were studied with reported median dose ingested 50 g (range 40–150 g). The median age was 28 years (range 13–78 years) and median presentation time 3.7 h (0.5–144 h). Activated charcoal was administered to 37 (25%), at a median time of 2 h post-ingestion (0.4–32 h). Two patients received charcoal after 24 h because of a second paracetamol peak. Acetylcysteine was given to 126 (87%), the median time to treatment was 6.5 h. In Australia, 300 mg/kg of intravenous acetylcysteine is given over 21 h; 50/126 (40%) requiring acetylcysteine received greater than 21 h of treatment. Of these 26 (21%) received additional acetylcysteine because paracetamol was still detected near the completion of the standard acetylcysteine infusion (paracetamol concentration range 3–1145 mg/L). Furthermore, 33 (26%) received an increased dose of acetylcysteine, most commonly a doubling of the 100 mg/kg over 16 h infusion. Hepatotoxicity occurred in 22 (15%), 5 treated within 8 h of ingestion; one received a liver transplant. A further 11 developed ALT  $> 50$  IU/L, 6 treated within 8 h. Median time to acetylcysteine was significantly longer in those developing an abnormal ALT (5.8 h versus 13.5 h,  $p < 0.001$ ). There was a significantly lower initial median paracetamol ratio, comparing those who received charcoal and those who did not (1.44 [ $n = 35$ ] versus 2.19 [ $n = 91$ ],  $p = 0.0002$ ). Only one patient receiving charcoal before 24 h developed an abnormal ALT (136 IU/L). Patients treated within 8 h of ingestion, who developed ALT  $> 50$  IU/L also had a significantly higher ratio (3.30 [ $n = 11$ ] versus 1.75 [ $n = 92$ ],  $p = 0.0003$ ). Overall there was no significant difference between groups in median dose ingested (50 g,  $p = \text{NS}$ ). Those requiring further acetylcysteine for detectable paracetamol, had a median paracetamol ratio of 3.02 (range 1.14–12.1). **Conclusion:** The Australian paracetamol guidelines recommend increasing the dose of acetylcysteine in patients with a paracetamol concentration double the nomogram line,<sup>[1]</sup> which was less likely in those given charcoal. A fifth required prolonged acetylcysteine treatment, because of detectable paracetamol at the completion of the standard infusion. This has implications for proposed shorter acetylcysteine regimens.

## Reference

- [1] Chiew AL, Fountain JS, Graudins A, et al. Summary Statement: New guidelines for management paracetamol poisoning in Australia and New Zealand. *Med J Aust.* 2015;203:215–218.

### 138. A multi-center, retrospective study to evaluate the safety and efficacy of a three-bag acetylcysteine dosing regimen compared to a two-bag acetylcysteine dosing regimen for the treatment of paracetamol overdose: The Danish Intravenous Acetylcysteine Study (DIVAS)

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**Objective:** The acetylcysteine regimen, although slightly variable worldwide, is universally complex; it includes three, separate, weight-determined infusions over different timeframes, with a resultant high risk of medication error.[1–3] In 2012, Denmark adopted a two-bag dosing regimen and it is recommended that all patients suspected of paracetamol poisoning are treated with acetylcysteine. The intent of this retrospective chart review is to collect efficacy and safety data of a two-bag dosing regimen for acetylcysteine infusion. **Methods:** A medical chart review of patients who received intravenous acetylcysteine for treatment of paracetamol overdose was conducted in two Danish medical centers from January 2012 through December 2014. Patients were identified using ICD-10 and Anatomical Therapeutic Chemical (ATC) Classification System codes. The REDCap system was used for electronic data acquisition and storage. **Results:** Of 490 cases, 147 were male (30%) with a mean age of  $42 \pm 18.7$  years and 343 were female (70%) with a mean age of  $33 \pm 18.1$  years. Acute ingestions comprised 82%, repeated ingestions were 16.7% and 1% were unknown. The three-bag regimen was administered to 133 (27.1%) cases and 357 cases (72.9%) received the two-bag regimen. Overall, 21 cases (4.3%) developed hepatotoxicity. Of the cases that received the two-bag regimen 15/357 (4.2%) developed hepatotoxicity while 8/133 (6.0%) of cases that received the three-bag regimen developed hepatotoxicity. The overall incidence of anaphylactoid reactions was 5.7% with all being mild to moderate in intensity. **Conclusion:** These data suggest comparable efficacy and safety between the two-bag and three-bag dosing regimens of acetylcysteine in paracetamol poisoning.

### References

- [1] Bateman DN, Dear JW, Thanacoody HK, et al. Reduction of adverse effects from intravenous acetylcysteine treatment for paracetamol poisoning: a randomised controlled trial. *Lancet*. 2014;383:697–704.
- [2] Ferner RE, Langford NJ, Anton C, et al. Random and systematic medication errors in routine clinical practice: a multicenter study of infusions, using acetylcysteine as an example. *Br J Clin Pharmacol*. 2001;52:573–577.
- [3] Hayes BD, Klein-Schwartz W, Doyon S. Frequency of medication errors with intravenous acetylcysteine for acetaminophen overdose. *Ann Pharmacother*. 2008;42:766–770.

### 139. Metal-on-metal hip joint prostheses: a retrospective case series investigating association of systemic toxicity with serum cobalt and chromium concentrations

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**Objective:** There has been increasing interest in the potential for toxicity associated with metal-on-metal (MoM) hip prostheses. We describe patients referred for outpatient clinical toxicology assessment of potential toxicity related to MoM prostheses. **Case series:** A retrospective review of patients with MoM hip joint prostheses from a specialist outpatient clinical toxicology service in London, UK and, the US Toxicology Investigator's Consortium (ToxIC) database. Thirty-one cases were identified (17 US, 14 UK); 8 (25.8%) had bilateral MoM prostheses; 3 (9.7%) had bilateral prostheses, of which one was MoM; 20 had unilateral MoM prostheses. All 31 had cobalt concentrations recorded (median peak cobalt concentration 10.0 [IQR 3.8–32.8] mcg/L); chromium concentration was recorded in 25 cases (median peak chromium concentration 6.9 [IQR 3.7–18.7] mcg/L). There was no difference in median concentration between those with unilateral and bilateral MoM for cobalt (10.0 [IQR 2.5–51.4] versus 10.2 [IQR 5.9–18.1] mcg/L;  $p = 0.73$ ) or chromium (9.1 [IQR 3.4–22.0] versus 6.7 [IQR 5.1–7.2] mcg/L;  $p = 0.47$ ). Twelve had joint magnetic resonance imaging (MRIs), of whom two (16.7%) had metallosis without correlation with cobalt/chromium concentrations (Fisher's exact test;  $p = 0.45$  and  $p = 0.18$ , respectively). The most commonly reported symptoms were lethargy/malaise and hearing loss (both reported by 9 (29.0%) individuals) (Table 1); the presence of symptoms did not correlate with cobalt/chromium concentrations. Three (9.7%) patients were diagnosed with significant systemic cobalt toxicity: median peak serum cobalt concentration (164.8 [IQR 87.6–630.4] mcg/L) was greater than those without this diagnosis (8.7 [IQR 2.8–18.1] mcg/L), but was not statistically significant ( $p = 0.056$ ).

**Table 1.** Frequency of clinical features by cobalt/chromium concentration in patients with metal-on-metal hip joint prostheses.

Clinical features	Number	Below median concentration*		Above median concentration*		p-value (Fisher's exact test)	
		Co	Cr	Co	Cr	Co	Cr
Numbness/paraesthesia	5 (16.1%)	1	0	4	2	0.33	0.48
Weakness/paralysis	3 (9.7%)	0	0	3	2	0.22	0.48
Peripheral neuropathy	2 (6.5%)	1	1	1	0	1.00	1.00
Lethargy/malaise	9 (29.0%)	4	5	5	2	1.00	0.37
Hearing loss	9 (29.0%)	5	5	4	1	1.00	0.15
Tinnitus	8 (25.8%)	4	1	4	2	1.00	1.00

\*Median peak cobalt (Co) concentration 10.0 mcg/L; median peak chromium (Cr) concentration 6.9 mcg/L

**Conclusion:** In these patients with potential toxicity related to MoM prostheses, although there was a high prevalence of reported symptoms, only three (9.7%) had significant cobalt toxicity. Symptoms did not correlate with peak cobalt/chromium concentrations and whilst cobalt/chromium concentrations were higher in those with systemic toxicity this difference was not statistically significant.

## 140. Metal release from hip implant: Clinical experience with N-acetylcysteine as potential complexing agent in two cases

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**Objective:** Local and systemic toxicity from cobalt (Co) and chromium (Cr) from metal-on-metal hip replacement may result in neuropathy, cardiomyopathy and hypothyroidism. However, consensus statements and evidence-based data on management of these patients are focused on hip implant-related problems with little information on toxicological management, including chelation. We describe two cases treated with N-acetylcysteine. **Case reports:** Case 1: In March 2012 a 67-year-old was male referred to our Poison Centre with high Co (16.06 mcg/L) and Cr (7.22 mcg/L) blood concentrations (normal values 0.05–1.1 mcg/L, Cr 0.1–0.5 mcg/L, respectively). In September 2009 he underwent Co/Cr hip implantation for coxarthrosis. Except for magnetic resonance that evidenced a little fluid collection near the acetabulum, orthopaedic evaluation and echography were normal. Oral N-acetylcysteine (300 mg/kg/day for 10 days) was given due to persistent elevation of blood concentrations. The Co/Cr blood concentrations dropped by 86% and 87%, respectively, after therapy and remained low during the 3 years' follow up. Case 2: In November 2013, an 81-year-old female was referred because of high Co (20.24 mcg/L) and Cr (4.25 mcg/L) blood concentrations. In January 2007 she had total hip metal arthroplasty. Clinical course was characterized by hip pain and peri-prosthetic fluid collection. No hip revision was indicated. Oral N-acetylcysteine (300 mg/kg/day for 9 days) decreased Co/Cr blood concentrations to 45% and 24% of the pre-chelation concentrations, respectively. In both cases increased urinary Co and Cr concentrations were observed during therapy. **Conclusion:** Toxicological management of patients with a metal prosthesis is complex and Co/Cr blood concentrations need to be evaluated. In patients with increased concentrations continuous exposure cannot be excluded and chelation could be considered, although described in few cases the efficacy of the chelating agents in these patients remains anecdotal.[1,2] N-Acetylcysteine with its thiol groups may provide complexing sites for metals,[3] and in our experience, was tolerated and reasonably increased Co/Cr elimination in two metal hip-implanted patients.

### References

- [1] Hannemann F, Hartmann A, Schmitt J, et al. European multidisciplinary consensus statement on the use and monitoring of

metal-on-metal bearings for total hip replacement and hip resurfacing. *Orthop Traumatol Surg Res.* 2013;99:263–271.

- [2] Bradberry SM, Wilkinson JM, Ferner RE. Systemic toxicity related to metal hip prostheses. *Clin Toxicol (Phila).* 2014;52:837–847.
- [3] Lobet JM, Domingo JL, Corbella J. Comparative effects of repeated parenteral administration of several chelators on the distribution and excretion of cobalt. *Res Commun Chem Pathol Pharmacol.* 1988;60:225–233.

## 141. Comparison of blood lead levels (BLL) in drug users, individuals under methadone maintenance therapy and healthy individuals

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**Objective:** Adulteration of opium with lead is a new health threat in Iran. There is widespread abuse of drugs in Iran and increasing reports of lead poisoning.[1–5] The aim of this study was to investigate the blood lead level (BLLs) in opium addicts and to compare it with the BLL in healthy individuals and those under methadone therapy. To our knowledge, it is the first study to investigate BLLs in patients under methadone maintenance therapy (MMT) in the literature. **Methods:** This case-control study was conducted in 99 participants in Birjand, Iran, consisting of 33 opium addicts, 33 patients under methadone therapy and 33 healthy individuals as controls. The BLL was measured in all participants and data analysis was done using SPSS 15. **Results:** There were 53 men and 46 women with a mean age of  $55.4 \pm 12.8$  years. The mean BLL in the opium addicts, methadone therapy group, and controls was  $80.3 \pm 34.5 \mu\text{g/L}$ ,  $67.9 \pm 25.4 \mu\text{g/L}$  and  $57.3 \pm 27.4 \mu\text{g/L}$ , respectively. There was a significant difference between the opium addicts and healthy individuals ( $p = 0.006$ ); but there was no significant difference in BLL between opium addicts and the methadone therapy group or between the methadone therapy group and the healthy group. Moreover the method of drug abuse (oral versus inhalational) had a significant effect on BLL ( $p = 0.036$ ), and a significant association was found between drug abuse duration and BLL. **Conclusion:** Overall, this study demonstrated a significant increase in BLL in opium addicts, particularly oral users, in comparison with healthy individuals.

### References

- [1] Malekinejad M, Vazirian M. Transition to injection amongst opioid users in Iran: Implications for harm reduction. *Int J Drug Policy.* 2012; 23:333–337.
- [2] Salehi H, Sayadi AR, Tashakori M, et al. Comparison of serum lead level in oral opium addicts with healthy control group. *Arch Iran Med.* 2009;12:555–558.
- [3] Farzin L, Amir M, Shams H, et al. Blood levels of lead, cadmium, and mercury in residents of Tehran. *Biol Trace Elem Res.* 2008;123:14–26.
- [4] Hayatbakhsh-Abbasi M, Ansari M, Shahesmaeili A, et al. Lead serum levels in opium-dependent individuals. *Addict Health.* 2009;1:106–109.
- [5] Domeneh BH, Tavakoli N, Jafari N. Blood lead level in opium dependents and its association with anemia: A cross-sectional study from the capital of Iran. *J Res Med Sci.* 2014;19:939–943.

## 142. Human accidental poisoning in a rural and fishing occupational setting in Italy: a 5-year Poison Control Center study

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**Objective:** To describe clinical aspects and medical management of human poisoning in a rural and fishing occupational setting, in order to identify preventive measures. **Methods:** A 5-year (2010–2014) retrospective study of data from the Pavia Poison Centre (PPC), which receives enquiries from all over Italy, was performed. Cases were evaluated for: circumstances of poisoning, clinical manifestations, management, risks factors and outcome. **Results:** Farmers, veterinarians, herpetologists, those involved in fishing and aquarists were identified as professionals at risk for accidental poisoning in a rural setting. In detail, 581 occupational poisoning cases were identified. These were: farmers (494; 87%) [pesticides/herbicides/rodenticides (439; 89%), insect/spider bites (9; 1.6%), *Vipera* envenomation (22; 4%) and lethal incident in confined spaces (8; 2%); veterinarians (64; 11.3%) [accidental self-administration of drugs/vaccine/antibiotics/sedatives (63; 98%), wound management for potential rabies (1, 2%); herpetologists (4; 0.7%) [*Agkistrodon bilineatus*, *Crotalus atrox*, *Bitis parviocula*, *Bothriechis schlegelii* envenomation]; fishing/aquarist (19; 3.4%) [stings, algal toxins intoxications, ciguatoxin ingestion, palytoxin inhalation]. The inappropriate and/or incorrect use of protective equipment was associated with toxic pesticide exposures. Envenomation by exotic snakes was rare and a particular risk for certain categories (e.g. herpetologists/veterinarians) and may require antivenom administration not always promptly available. In these cases specific antidote was obtained from abroad after activation of extraordinary procedures. All cases fully recovered except one (*Crotalus* bite) that had a mild permanent dysfunction of the hand. Among veterinarians, occupational exposures are mainly characterized by accidental self-injection of veterinary medicines. No cases of systemic toxic effects were registered. The veterinarian managed for a potentially rabid fox bite required only active immunization. In the PPC experience fishermen may be exposed to stings from venomous marine organisms (Trachinidae 50%, Dasyatidae 25%, moray eel 13%, sea anemone/coral 12%). Aquarists were exposed to palytoxin inhalation after boiling a pot of water containing a piece of rock polluted by the cnidarian zoanthids *Palythoa* species, removed from a 300 L aquarium. The patients (father 36-years-old and daughter 18-months) manifested gastrointestinal symptoms, fever (39°C), sore throat, cough and dyspnea. They had recovered by 48 hours. **Conclusion:** Besides playing a fundamental role in the diagnosis of intoxication, the PPC also provides specialized advice to evaluate correct indications for antidote administration and to supply antidote in an adequate quantity. In occupational settings, a correct preventive information program may be essential and continuous training of physicians and workers is required.

## 143. Validation of a prediction rule for adverse cardiovascular events from drug overdose

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**Objective:** Adverse cardiovascular events (ACVE) complicate up to 16.9% of hospitalizations in acute drug overdose patients.[1] We previously derived a risk prediction rule for ACVE in patients with acute drug overdose that had a 97.1% negative predictive value,[2] and sought to internally validate that rule. **Methods:** A prospective cohort study conducted over 17 months (2012–2014) at two urban university hospitals. Patients were adults with suspected acute drug overdose enrolled from the emergency department. The composite study outcome, ACVE, was defined as any of the following: myocardial injury (elevated cardiac troponin I), shock (requiring vasopressors), ventricular dysrhythmia (tachycardia or fibrillations, torsades de pointes), or cardiac arrest (pulselessness requiring cardiopulmonary resuscitation [CPR]). The risk prediction rule included any of these 3 factors: prior cardiac disease (coronary artery disease or congestive heart failure); QTc  $\geq 500$  ms; initial serum bicarbonate  $\leq 20$  mmol/L. Sample size was predetermined in order to calculate the rule test characteristics with 95% confidence interval (CI) widths  $< 5\%$ ; we calculated the need to analyze 900 patients. **Results:** There were 1457 suspected acute drug overdose patients screened, of whom 552 were excluded (185 non-drug overdose, 145 pediatrics, 111 missing data, 110 alternate diagnosis, 1 chronic), leaving 905 for analysis (mean age 41 years; female, 44%; suicidal, 40%). ACVE occurred in 65 patients (7.2%, CI 5.6–9.1) (myocardial injury 44; shock 31; dysrhythmia 16; cardiac arrest 17) and there were 16 deaths (1.8%, CI 0.9–2.6). The multivariable model adjusting for the previously derived risk factors, controlling for age, confirmed the following independent predictors of ACVE: QTc  $\geq 500$  ms (OR 5.5, CI 2.8–10.9), bicarbonate  $\leq 20$  mmol/L (OR 2.7, CI 1.5–4.9), and prior cardiac disease (OR 39.5, CI 17.9–87). The validated prediction rule had 75.4% (CI 63.1–85.2) sensitivity, 82.3% specificity (CI 79.9–85.1), and 97.8% negative predictive value (CI 96.4–98.7). The presence of 2 or more risk factors had 51.5% positive predictive value (CI 34.5–68.6). **Conclusion:** Validation of the previously-derived risk prediction rule for ACVE in patients with acute drug overdose demonstrated slightly improved sensitivity and negative predictive value in the validation cohort. External validation in distinct patient populations and clinical settings remains warranted.

### References

- [1] Manini AF, Nelson LS, Stimmel B, et al. Incidence of adverse cardiovascular events in adults following drug overdose. *Acad Emerg Med.* 2012;19:843–849.
- [2] Manini AF, Hoffman RS, Stimmel B, et al. Clinical risk factors for in-hospital adverse cardiovascular events after acute drug overdose. *Acad Emerg Med.* 2015;22:499–507.

## 144. Antagonizing the errors of history: bedside experience with flumazenil

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**Objective:** Toxicity from sedatives negatively affects cognition, behavior, and physiologic status. Although a direct antidote is available, it is rarely used due to fears of withdrawal and seizures. Flumazenil is approved for treatment of sedation and/or coma secondary to GABA-ergic substances. It has been proposed for cases of unresponsiveness of unknown etiology and has also been effective in reversing paradoxical reactions to benzodiazepines,<sup>[1]</sup> but flumazenil remains underutilized in clinical practice due to clinical lore and case reports of adverse events. At one toxicology center, however, flumazenil is routinely employed in the emergency department and acute hospital settings. It is administered 0.5 mg IV over 30 seconds, repeated every 1–2 hours as required to sedated and/or confused patients with relaxed autonomic indices and peripheral neurologic status. This study was designed to systematically report on the safety and efficacy of that practice. **Methods:** A six-year retrospective review of antidote use and a one-year close observational study of critical care toxicology practice in a toxicology center. Retrospective cases were identified through keyword searches of electronic medical and pharmacy records, correlated with written service records for all 5063 patients seen from 2003–2010. Prospective cases were collected as part of standard clinical practice by study investigators from 2010–2011, with intentional gathering of data on toxicologic diagnoses, medical histories, antidotal responses and adverse effects. **Results:** Flumazenil was used to treat 731 patients over the two phases of study. The overall positive response rate was over 80%. No major adverse events were documented for the entire retrospective period. In the prospective year, there were 12 instances of minor side effects out of 212 patients treated. No seizures, arrhythmias, or episodes of emesis were observed. Three patients experienced drooling, 7 had transient anxiety, and there were 2 separate episodes of odd behavior upon awakening from coma in a patient with central nervous system (CNS) disease and Cluster B personality disorder. Comorbid anxiety disorders were associated with anxiety after flumazenil treatment, but no patient required medical intervention for this effect. **Conclusion:** Flumazenil is a safe diagnostic and therapeutic antidote for cases of suspected toxic sedation. Concerns about treating patients with seizure disorders and/or chronic use of benzodiazepines are unfounded based on our data. Side effects are rare and mild, and can be managed with caregiver presence and behavioral interventions.

### Reference

- [1] Weinbroum AA, Flaishon R, Sorkine P, et al. A risk-benefit assessment of flumazenil in the management of benzodiazepine overdose. *Drug Saf.* 1997;17:181–196.

## 145. Effectiveness of correction of metabolic acidosis on intermittent versus continuous modes of hemodialysis in acute methanol poisoning

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**Objective:** Severity of metabolic acidosis is a well-known prognostic parameter in acute methanol poisoning. A strong association exists between arterial blood pH and mortality and probability of long-term sequelae of poisoning. During an outbreak of methanol poisonings in the Czech Republic in 2012, we studied the effectiveness of acidemia correction with intermittent/extended daily hemodialysis (IHD/EDD) versus continuous veno-venous hemofiltration/hemodialysis/hemodiafiltration (CVVH/HD/HDF). **Methods:** Data were obtained from a prospective study on 31 patients treated with dialysis: IHD was used in 13, EDD in 5, and CVVH/HD/HDF in 13 patients. The mean time needed for a 0.01 increase in arterial blood pH, a 1 mmol/L increase of standard bicarbonate, and the total time to standard bicarbonate correction ( $\geq 22$  mmol/L) during dialysis session, were measured. **Results:** The CVVH/HD/HDF group was more acidotic than IHD/EDD group (mean pH  $6.79 \pm 0.1$  versus  $7.05 \pm 0.1$ ,  $p = 0.001$ ). No correlation between measured parameters of acidemia correction and age, weight, and serum methanol concentration on admission was found. The total time to standard bicarbonate correction correlated with arterial blood pH ( $r = -0.511$ ;  $p = 0.003$ ), serum glucose ( $r = 0.399$ ;  $p = 0.026$ ), and lactate on admission ( $r = 0.383$ ;  $p = 0.040$ ). The mean time to 1 mmol/L-increase of standard bicarbonate was  $0.193 \pm 0.033$  hours for IHD/EDD and  $0.570 \pm 0.140$  hours for CVVH/HD/HDF ( $p < 0.001$ ), and the mean time needed to 0.01 increase of arterial blood pH was  $0.113 \pm 0.019$  hours for IHD/EDD and  $0.189 \pm 0.061$  hours for CVVH/HD/HDF ( $p = 0.024$ ). The mean rate of increase of standard bicarbonate was  $5.67 \pm 0.90$  mmol/L/hour for IHD/EDD and  $2.17 \pm 0.74$  mmol/L/hour for CVVH/HD/HDF ( $p < 0.001$ ). The mean time needed for 1 mmol/L increase of standard bicarbonate correlated with dialysate flow rate ( $r = -0.657$ ;  $p < 0.001$ ) and blood flow rate ( $r = -0.460$ ;  $p = 0.009$ ). The total time to standard bicarbonate correction correlated with dialysate flow rate ( $r = -0.738$ ;  $p < 0.001$ ) and blood flow rate ( $r = -0.602$ ;  $p < 0.001$ ). The mean time needed for 0.01 increase of arterial blood pH was 40% shorter and the mean time to 1 mmol/L increase of standard bicarbonate was more than 60% shorter with IHD/EDD compared to CVVH/HD/HDF, and resulted from the higher blood and dialysate flow rates on intermittent mode of dialysis. **Conclusion:** Our study supports the superiority of IHD/EDD over CVVH/HD/HDF in terms of rate of metabolic acidosis correction. We recommend optimizing dialysis by increasing the blood and dialysate flow as much as possible given the limitations of the apparatus and the patient's clinical conditions. **Acknowledgements:** Charles University projects P25/1LF/2, P26/1LF/2, and P28/1LF/6.

## 146. Outbreak of facio-truncular dystonia in central Africa due to falsified diazepam containing haloperidol

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**Objective:** In December 2014, patients with suspected meningitis were reported by the Ituri Health District, in the northeast Democratic Republic of Congo. In January 2015, Médecins sans Frontières (MSF) was approached by the Ministry of Health (MoH) to support outbreak investigation and response. **Methods:** At MoH and MSF case-management sites, information for each patient was recorded in a standardized Excel line-list. Patients' demographic characteristics, clinical features, and outcome are described. Cerebrospinal fluid (CSF) was analysed for evidence of meningitis, and urine and 39 medicine samples underwent toxicological investigations. **Results:** Initial investigations suggested that bacterial meningitis was not the aetiology. The epidemiological pattern of the outbreak (curve, age distribution, evolution), the negative clinical symptoms/signs for meningitis (few with fever, neck stiffness, Kernig's or Brudzinski's signs), the fact that only four patients had CSF evidence for *Neisseria meningitidis*, the clinical features of acute dystonia, the very low mortality and absence of severe sequelae, the clinical improvement with diazepam and the good outcome without antibiotics suggested, on 4 February 2015, that bacterial meningitis was not the cause of this outbreak. Patients presented with acute dystonic reactions affecting the muscles of the face, eyes, neck, tongue, and upper limbs with Parkinsonism and oculogyric crises. Over eight months, there were 1029 hospitalisations (931 patients with at least one admission). When videos of patients were reviewed by paediatric neurologists, they suggested "facial-truncal dystonic reaction". This insight changed the strategy of investigation from an outbreak of suspected meningitis to an outbreak of unknown origin resulting in acute dystonic reactions, probably linked to a toxic agent causing extrapyramidal reactions. The urine from all patient samples tested positive for haloperidol. Analysis of medicine samples demonstrated that one type of tablet sold as "diazepam" contained haloperidol as the sole active pharmaceutical ingredient, suggesting that this large outbreak was due to haloperidol toxicity from falsified diazepam. How diazepam came to contain haloperidol is still under investigation by national/international authorities. **Conclusion:** This outbreak emphasizes the need to consider toxicity resulting from falsified medicines when facing collective atypical signs and symptoms. To address such outbreaks, an international multidisciplinary collaboration, including clinical toxicologists, working in collaboration with medicine regulatory authorities are mandatory to address the major challenge of falsified drugs in developing countries.

## 147. To what extent does haloperidol-induced facio-truncular dystonic syndrome mimic infectious diseases? The Congo experience

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**Objective:** From week 52 in 2014 to August 2015 there was an outbreak of atypical meningitis in the North-East of the Democratic Republic of Congo, an area included in the "meningitis belt" of Africa. Médecins Sans Frontières (MSF) was asked to provide evidence that clinical findings did not result from an infectious disease but rather from a toxicological origin, actually a facio-truncular dystonic syndrome (FTDS) resulting from haloperidol replacing diazepam in medications. **Methods:** To address this major issue, data were collected at the outbreak epicentre in order to allow comparison of FTDS and infectious diseases using individual chart file records, examination of patients at the site, and administration of biperiden. In patients without sepsis, antibiotics were withdrawn. FTDS was evidenced by positive urine toxicological analysis. **Results:** From weeks 1–13, 2015, there were 158 consecutive cases of FTDS, the ratio of patients of < 5 years versus greater was 20/80%. There were no deaths. The weekly increase in cases was hectic. In the MSF centre at Atsinia, 11 cases of FTDS were collected meanwhile 10 patients were admitted for infectious diseases, including meningitis, malaria or both. In the FTDS and infectious groups, the median of age (range) were 16 years (0.5–45) and 10 years (0.5–42), respectively. The M/F sex ratio were 2/9 and 5/5. The median delay in onset of signs and symptoms were 1 day (0.5–3) and 2 days (1–3), respectively. The frequencies of signs and symptoms in the FTDS and infectious groups were: muscle stiffness (91%/70%), neck stiffness (64%/70%), protrusion of the tongue (64%/20%), headache (45%/9%), facial distortion (36%/0%), upright deviation of the eyes (27%/30%) and seizures (18%/20%). Regarding signs of sepsis, the median temperature on admission was 37°C (36–38) and 38°C (35.5–38.9). Systemic inflammatory response syndrome (SIRS) indexed by age was noted in 1/11 (9%) and 4/10 (40%) of cases in the FTDS and infectious groups, respectively. Finally, biperiden was consistently efficient in cases of FTDS who recovered without antibiotics. **Conclusion:** These results suggest great similarity of signs and symptoms between FTDS and meningitis including, delay in onset, headache (more frequent in FTDS than meningitis), neck stiffness, upright deviation of the eyes, and seizures. However, there were also major differences including rapid increase in the weekly number of cases, sensitivity of females, the number of adults presenting with FTDS, protrusion of tongue and facial distortion. FTDS presented without SIRS in the majority of cases and was reversed by biperiden.

## 148. Abuse of immediate release opioid analgesics as compared to extended release formulations in the US

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**Objective:** Therapeutic use and subsequent abuse of prescription opioids in the US increased substantially between 1990 and 2010.[1] However, promising data show multiple recent interventions may contribute to a decrease in prescription opioid abuse.[2] The US market share of opioid analgesics is 10% extended release (ER) and 90% immediate release (IR). However, most interventions have focused on decreasing ER abuse. Our objective was to compare rates of opioid analgesic abuse for ER and IR formulations in the US using poison center data. **Methods:** We compared rates of abuse of ER to IR opioid formulations using data from the Research, Abuse, Diversion and Addiction Related Surveillance (RADARS<sup>®</sup>) system Poison Center Program. Data for



opioid intentional abuse were evaluated from 2009 through 2014, and Poisson regression was used to compare IR opioid case counts and ER opioid counts over time. **Results:** From 2009 to 2014, the rate of IR opioid abuse adjusted for population was markedly higher than the rate of ER abuse, with an IR rate in 2014 of 0.179 (0.165–0.194) per 100,000 population, and an ER rate of 0.023 (95% CI 0.019–0.029). The population-adjusted rates for both ER and IR abuse declined, with ER decreasing by 7.4% and IR decreasing by 5.2% by 2014. When adjusted for prescriptions dispensed, the rate of ER abuse was higher than the rate of IR abuse, with an ER rate of 0.213 (0.176–0.257) per 10,000 prescriptions, and an IR rate of 0.107 (0.099–0.115). However, the rate of ER abuse declined significantly more rapidly than the IR rate, with an 8.3% decrease by 2014 for ER abuse and a 3.8% decrease for IR abuse. **Conclusion:** Between 2009 and 2014, rates of prescription opioid abuse per population were higher for IR medications than ER medications, with the rates for both declining during that time. However, when adjusted for prescriptions dispensed, the rates for ER medications were higher than those for IR medications, but with the rates for ER medications declining more rapidly. For a larger public health impact, interventions to decrease prescription opioid abuse in the US should include both IR and ER formulations.

## References

- [1] The DAWN Report: Highlights of the 2011 Drug Abuse Warning Network (DAWN) Findings on Drug-Related Emergency Department Visits. SAMHSA 2014; [cited 2016 Feb 24]. Available at: <http://archive.samhsa.gov/data/2k13/DAWN127/sr127-DAWN-highlights.htm>
- [2] Dart RC, Surrat HL, Cicero TJ, et al. Trends in opioid analgesic abuse and mortality in the USA. *N Engl J Med.* 2015;372:241–248.

## 149. Ingestion of codeine syrup in children: a 10-year retrospective study

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**Objective:** Codeine bound to polystyrene sulfonate in syrup has been prescribed frequently for children to relieve cough. Since July 2015 codeine is contraindicated for the treatment of cough in paediatric patients younger than 12 years in Austria, because metabolism is variable and unpredictable in this age group, increasing the risk of side effects. **Methods:** We evaluated telephone enquiries to the Poisons Information Centre (PIC) in Austria regarding intake of codeine bound to polystyrene sulfonate by children under the age of 14 years from 2005 to 2014. **Results:** The PIC received 300 calls related to 260 children (aged between 45 days and 14 years); 40 of the enquiries were repeated calls. In 41 cases the children's weight or the amount suspected could not be defined. The remaining 219 children ingested codeine either unintentionally on their own ( $n = 186$ ; 85%) or a wrong dose was given by a parent ( $n = 33$ ; 15%). According to the literature<sup>1</sup> and our own data a threshold value of 5 mg/kg was chosen for analysis as an estimated limit for the probability of a relevant intoxication. In 125 cases (93 accidental, 32 mistakenly given by a parent) the amount of codeine ingested was under 5 mg/kg. In 123 (98.4%) of these cases there were no signs of intoxication. In one case the risk of intoxication could not be estimated at the time of consultation. One child (9 months, 6.8 kg) became somnolent after a calculated dosage of 1.7 mg/kg, however in this case the syrup was old, not properly closed and had thickened. In

94 cases (93 accidental, 1 mistakenly given by a parent) the amount of codeine ingested was over 5 mg/kg. In 27 (28.7%) of these cases intoxication could be excluded, in 8 (8.5%) patients the risk could not be estimated. In 59 (62.8%) cases hospitalization was recommended. In children that ingested >5 mg/kg 13 (13.8%) developed symptoms such as fatigue ( $n = 6$ ), vomiting ( $n = 6$ ), nausea ( $n = 1$ ), miosis ( $n = 1$ ), somnolence ( $n = 1$ ), and agitation ( $n = 1$ ). **Conclusion:** The recommendation for medical monitoring after ingestion of >5 mg/kg of codeine bound to polystyrene sulfonate is confirmed by our evaluation. However, special care is necessary if correct storage and usage cannot be confirmed.

## Reference

- [1] Schlatter-Lanz I, Schneider L. [Vergiftungen mit opioidhaltigen Hustenmitteln]. *Schweiz Apotheker Zeitung.* 1989;127:645–648.

## 150. Rebound hepatotoxicity following successful treatment of acetaminophen overdose

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**Objective:** To report a case of clinically significant rebound hepatotoxicity following appropriate treatment for an acetaminophen overdose. **Case report:** A 14-year-old female presented with severe vomiting 8 hours after she reportedly ingested 94 tablets of 325 mg acetaminophen (30.55 g) and six tablets of 200 mg ibuprofen. Her initial vital signs were stable and her acetaminophen concentration upon arrival to the emergency department was 262.7 mcg/mL, aspartate aminotransferase (AST) was 34 IU/L, and alanine aminotransferase (ALT) 108 IU/L. Other laboratory values were not consistent with coagulopathy, renal injury, or acidosis. She was immediately started on a 21 hour treatment course of intravenous N-acetylcysteine (150 mg/kg intravenous bolus over 1 hour followed by 50 mg/kg intravenous over 4 hours and then 100 mg/kg intravenous over 16 hours). Following treatment, repeat laboratory values demonstrated an acetaminophen concentration less than 10 mcg/mL, AST 32 IU/L, and ALT 40 IU/L and N-acetylcysteine was subsequently discontinued. The next morning while awaiting psychiatric consult, the patient's vomiting returned. Repeat laboratory tests obtained 24 hours after N-acetylcysteine had been discontinued showed ALT 146 IU/L, AST 135 IU/L, N-acetaminophen was undetectable, and bilirubin was 0.3 mg/dL. Due to rebound hepatotoxicity, a repeat course of N-acetylcysteine was commenced (with the same regimen as previously). AST peaked at 205 IU/L and ALT peaked at 395 IU/L. The patient never had any coagulopathy, acidosis, or renal insufficiency. Repeat liver function tests were checked after the second treatment round of N-acetylcysteine was completed and were within the normal reference range. **Conclusion:** This case is unique in that it demonstrates an initial mild hepatic injury as demonstrated by the admission ALT of 108 IU/L with subsequent resolution of symptoms, successful metabolism of acetaminophen, and return of hepatic function markers to normal, followed 48 hours after ingestion, with laboratory and clinical symptoms consistent with a rebound hepatic injury. There was no exposure to other hepatotoxic agents and her acetaminophen concentration remained undetectable. A second course of N-acetylcysteine was started with successful resolution of the patient's hepatic injury. Further research may be necessary to determine if prolonged surveillance of hepatic function is required following acetaminophen toxicity.

## 151. Paracetamol poisonings treated with two complete courses of N-acetylcysteine

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**Objective:** Peak paracetamol concentrations sometimes occur extremely late in the course of exposure after a single overdose. In some of these cases, the question arises whether the regular dosing schedule of N-acetylcysteine (NAC), which after the first 4¼ hours of treatment is reduced to 6.25 mg/kg/h, is inadequate. We report two cases with very late peak paracetamol concentrations where the NAC treatment schedule was restarted. **Case reports:** Case 1: A 48-year-old male was admitted to hospital shortly after ingestion of 105 g paracetamol and high doses of opioids (6.3 g codeine, 550 mg ketobemidone). He presented unconscious with pronounced opioid symptoms. NAC infusion was started immediately. Liver function tests were normal. The initial plasma paracetamol concentration was 1197 µmol/L, decreasing to 308 µmol/L 16 hours after admission. However, at 32 hours there was a second peak concentration of 1315 µmol/L. It was presumed that the absorption of paracetamol had been delayed due to reduced gastrointestinal motility. At 34 hours, it was therefore decided to restart the NAC treatment schedule (ongoing at 6.25 mg/kg/h) with the regular initial bolus dose (150 mg/kg/15 min) followed by 50 mg/kg/4 h and 100 mg/kg/16 h. The patient developed significant liver damage with a peak ALT of 34.3 µkat/L (2060 U/L) at 120 hours (INR 1.2). Case 2: Another 48-year-old male ingested 66.5 g paracetamol in the form of modified-release tablets. He also presented to hospital about one hour later and the initial paracetamol concentration was 1032 µmol/L. Liver function tests were normal. NAC was started immediately. Subsequent paracetamol concentrations rose to 2871 µmol/L 18 hours after admission. At that point, it was decided to restart the NAC treatment with a second full course as in case 1. The patient developed liver damage with a peak ALT of 111 µkat/L (6660 U/L) at 113 hours (INR 2.0). **Conclusion:** These two cases illustrate the problem with delayed peak paracetamol concentrations. Both patients had a long period of high paracetamol concentrations during which they only received a NAC dose of 6.25 mg/kg/h (prolonged third bag). This fact may reasonably explain the development of liver damage despite the rigorous treatment. Serial paracetamol measurements and timely appropriate dosage adjustment of NAC are suggested in selected cases.

## 152. Pregabalin overdose: a review of cases reported to a poisons centre

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**Objective:** Pregabalin is a gamma-aminobutyric acid (GABA) analogue approved for the treatment of partial seizures, neuropathic pain and generalised anxiety disorder. It has also been used to potentiate the effects of recreational drugs.[1] The aim of this study was to review the circumstances of exposure and the severity of poisoning following pregabalin overdose. **Methods:** A retrospective review of enquiries to the National Poisons Information

Centre (NPIC) concerning pregabalin in patients 16 years and older from 2009 to 2013 inclusive was conducted. Data extracted included gender, age, coingestants, route of exposure, circumstances (intent), poisoning severity score (PSS), and features of poisoning. **Results:** In total 482 cases were reviewed (286 female, 196 male). The mean age of patients was 38 years with 67.3% between the age of 20 and 49 years. Most enquiries (78.8%) concerned intentional overdose of pregabalin, with 15.3% accidental overdose/therapeutic errors, 1.5% recreational abuse and 4.4% other/unknown intent. Pregabalin was the only substance taken in 103 cases (21.4%) while the majority of patients (78.6%) had taken multiple agents. The most common coingestants were benzodiazepines (41.1%), antidepressants (32.2%), antipsychotics (26.6%) and alcohol (15.8%); 64 patients (13.3%) had also taken opiates, including 11 who had taken heroin. Also 8 (1.7%) patients had taken CNS stimulants and 3 (0.6%) cannabis. Intentional overdose of pregabalin alone occurred in 57 patients; 24 of these cases were asymptomatic, 23 had minor features, 4 moderate and 2 severe features of poisoning. Features were not known in two cases and two patients had symptoms attributed to their psychiatric illness. Drowsiness was the most common feature reported ( $n = 17$ ). Other features were tachycardia ( $n = 5$ ), vomiting ( $n = 3$ ), dizziness ( $n = 2$ ) and coma ( $n = 2$ ). Abdominal pain, nausea, diarrhoea, mild haematemesis, tremor, ataxia, confusion, hallucinations, hypertension, neck stiffness and sweating were also reported (1 case each). Convulsions were reported in two patients but were unwitnessed in one case and pseudoseizures were suspected in the second. Two fatalities were reported following pregabalin overdose and both were associated with other coingestants. **Conclusion:** Recreational use of pregabalin was rarely reported (1.5%) and only a small number of patients had also taken illegal drugs. Drowsiness was the most common feature reported following intentional overdose of pregabalin alone. Severe toxicity was rare and the two fatalities reported followed mixed overdoses.

### Reference

- [1] Schifano F. Misuse and abuse of pregabalin and gabapentin: cause for concern? *CNS Drugs*. 2014;28:491–496.

## 153. Attacks with self-defense sprays

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**Objective:** The use of defense sprays, most of which contain CS, CN or oleoresin capsicum (OC) as the active agent, is common in many countries.[1] However, these sprays may be used as offensive weapons during a fight or a robbery.[2] The aim of this study was to describe the characteristics of patients treated by our emergency department after an assault with a self-defense spray. **Methods:** We reviewed all patients who attended the Chemical Decontamination Unit (CDU), Emergency Department, Hospital Clinic of Barcelona, in 2010–2014. Patients assaulted by a self-defense spray were selected. Epidemiological, clinical, and therapeutic features and the evolution were evaluated. **Results:** Fifteen patients, representing 13% of cases that attended the CDU, were included. The mean age was 25 years, 13 (87%) were male and 53% of cases were foreigners in Barcelona for work, family or tourism. In all cases, the assault occurred during a fight or an attempted robbery. Sixty-seven per cent of cases occurred

between 04:30 and 06:30 hours, and in 60% of cases  $\geq 2$  patients attacked in the same episode were treated. The location of the attack was in the street (67%), inside a nightclub (20%) or a commercial property (7%). The most-affected areas were the face and eyes. The predominant symptoms were itching, irritation, burning sensation and pain. Treatment was an amphoteric, osmotic solution in 80% of cases, and water or saline solution in other cases, achieving a significant symptomatic improvement. Reported pain was measured using a visual analog scale, and decreased from a mean of 7 points at admission to 3 points after decontamination ( $p < 0.01$ ). Eleven cases required ophthalmological care consisting of topical symptomatic treatment. There were no sequelae in any case. **Conclusion:** The use of self-defense sprays in assaults or robberies is a reality in our environment. Decontamination measures help relieve symptoms and the prognosis is good.

## References

- [1] Dueñas A, Felipe S, Ruiz-Mambrilla M, et al. CO poisoning caused by inhalation of  $\text{CH}_3\text{Cl}$  contained in personal defense spray. *Am J Emerg Med.* 2000;18:120–121.
- [2] Breakell A, Bodwala GG. CS gas exposure in a crowded night club: The consequences for an accident and emergency department. *J Accid Emerg Med.* 1988;15:56–57.

## 154. Death after imidacloprid ingestion: a case report

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**Objective:** Imidacloprid belongs to a relatively new class of insecticides, the chloronicotinyl neonicotinoid compounds. Animal studies indicate relatively low toxicity to mammals.[1] Imidacloprid, the commonest neonicotinoid used in South Asia, was recently reported to have a 0% case fatality in a series of 68 patients presenting with poisoning.[2] Here we report death after ingestion of imidacloprid. **Case report:** A 28-year-old male was brought to our emergency department with a history of intentional ingestion of about 250 ml of 14% imidacloprid two hours prior to arrival. He was agitated and developed nausea, vomiting, dilated reactive pupils with muscle jerking movements. He had no significant co-morbid medical illness or any addiction. On physical examination his temperature was  $36.7^\circ\text{C}$  with heart rate 98/min, blood pressure 110/60 mmHg, respiratory rate 18/min and oxygen saturation of 92%. His oxygen saturation and heart rate decreased 90 minutes after admission and he developed apnoea. After intubation, administration of 0.5 mg atropine, and transfer to the intensive care unit he had tachycardia 160/minute and hyperthermia  $38.9^\circ\text{C}$ . Supportive care was initiated. Investigations showed that he had leukocytosis with normal hemoglobin, and erythrocyte and platelet counts. His electrocardiogram showed normal sinus tachycardia and serum electrolytes, blood sugar, creatine phosphokinase (CPK), lactate dehydrogenase (LDH), aminotransferases, arterial blood gas, kidney function tests and cholinesterase activity were normal. Intravenous midazolam was given but failed to control jerking movements of the lower and upper limbs and a propofol infusion was started. Approximately 30 minutes later the patient had a cardiac arrest. He responded to 10 minutes of cardiopulmonary resuscitation (CPR) with an adequate pulse rate but unfortunately two hours later had another arrest and died. **Conclusion:** This patient manifested neurogenic and cardiopulmonary dysfunction probably due to

central nicotinic stimulation, but these symptoms are not considered characteristic and specific for imidacloprid poisoning. In this patient progressive deterioration and eventual demise could not have been predicted. A serum imidacloprid concentration would have helped confirm exposure but was unavailable. This report of imidacloprid toxicity sensitizes clinicians to an emerging cause of poisoning and highlights the need for a careful review of its toxicity profile.

## References

- [1] Shadnia S, Moghaddam HH. Fatal Intoxication with imidacloprid insecticide. *Am J Emerg Med.* 2008;26:634.
- [2] Mohamed F, Gawarammana I, Robertson TA, et al. Acute human self poisoning with imidacloprid compound: a neonicotinoid insecticide. *PLoS One.* 4:e5127.

## 155. Fatal accidental ingestion of alphachloralose rodenticide in two siblings

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**Objective:** Alphachloralose is used as a rodenticide. The compound is formed from the chemical combination of equimolar chloral and glucose and was first synthesized in 1889 by Heffter.[1] In Morocco various products are available as grains, paste, powder or blocks 'packaged in packs of 3 g, 7 g or as 9 g (three packs of 3 g). Product names include Raticide 50, Raticide 70, Black Pearl Grains and Alfa Ratone Block. **Case report:** We report the case of two siblings, a girl of 6-years-old and her 3-year-old brother. The children were brought to the emergency room of a provincial hospital with suspected food poisoning. The father reported that the offending food was a dairy product that the children had consumed an hour before. On admission both children had intractable vomiting and abdominal pain. The girl also had severe diarrhea. Neurologically they were very agitated with impaired consciousness, bradycardia (50 beat by minutes) and cyanotic lips. They were given an intravenous infusion of sedative and antiemetic drugs but they died a few hours after admission. In view of this event, the Ministry of Health decided to open an investigation after taking toxicology samples from the children. An analysis of the remains of the offending food was negative, however, after examination and inspection of the family home, the investigation revealed the use of a rodenticide "Raticide 50". The previous day the mother had deposited the bait on pieces of bread and tomato slices behind a closet that was easily accessible to children. The conclusion was that the children were victims of accidental poisoning by rat poison. **Conclusion:** We report the fatal poisoning of two siblings by an alphachloralose rodenticide. This product is widely used at home by the Moroccan population and is responsible for a significant number of poisoning cases, mostly in infants. Unrestricted sale, ease of access, cheap price and lack of awareness means that the number of poisoning cases is increasing and currently poses a health problem requiring a multi-strategic response.

## Reference

- [1] Stoupe N, Monseu G, Cnockaerts P. [Human intoxication by chloralose. Clinical study and electroencephalography.] [Article in French] *Acta Neurol Belg.* 1970;70:352–358.

## 156. Methanol and formate concentrations in brain after methanol poisoning

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**Objective:** Methanol poisoning is known to cause visual disturbances and cerebral damage, predominantly affecting the basal ganglia. Mitochondrial toxicity from formate, the ultimate metabolite of methanol in humans, is believed to be the mechanism. A prerequisite would be that concentrations of formate in the central nervous system reach values that are likely to exert such toxic effects. We therefore ventured to measure methanol and formate in the central nervous system of persons who had died from methanol poisoning. **Methods:** Blood and tissue material was collected according to a prospective protocol from autopsy of two patients that had died from methanol poisoning in Estonia. Samples were dissected and homogenized, and the post-mitochondrial supernatant was analysed for methanol and formate with a newly developed gas chromatography-mass spectrometry (GC-MS) method (to be published). **Results:** Methanol and formate were measurable in all tissues tested. Concentrations in the cortex and basal ganglion were similar. Methanol and formate concentrations were higher in the brain than the blood. In one patient the formate concentration in the brain was higher than the blood concentration and in the other patient the blood concentration was greater (Table 1). **Conclusion:** As formate and methanol are unlikely to be bound to tissues, the different brain-to-blood ratios suggest that the patients died in different toxicokinetic phases of methanol poisoning. Results from autopsy material must be interpreted with caution because they represent only a snapshot in a highly dynamic process where brain-to-blood and CSF-to-blood ratios may vary greatly. There is no indication from this pilot study that there are large regional variations in methanol and formate concentrations within the brain. We aim to follow up this study with more patient samples and a more sophisticated dissection of the brain samples before analyses to reduce potential sources of error.

**Table 1.** Methanol and formate concentrations in two fatal cases of methanol poisoning.

Tissue	Patient 1		Patient 2	
	Methanol (mmol/L)	Formate (mmol/L)	Methanol (mmol/L)	Formate (mmol/L)
Full blood	8	2	5	11
Brain (cortex)	29	4.3	53	3.9
Brain (basal ganglion)	38	6.1	59	4.1
Cerebrospinal fluid (CSF)	–	–	40	8.1

## 157. Severe hypertension and bradycardia secondary to midodrine overdose

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**Objective:** Midodrine is a peripherally acting alpha-1 agonist used to treat conditions such as orthostatic hypotension and dialysis-associated hypotension.[1,2] It is well absorbed via the gastrointestinal route (oral bioavailability 93%) and rapidly metabolized to an active metabolite desglymidodrine. Early studies measured desglymidodrine peak plasma concentrations in 60–90 minutes. There are no reports measuring serum midodrine concentrations in overdose or patients with a hypertensive crisis. We present the case of a patient who overdosed on midodrine resulting in severe hypertension requiring intensive care admission. **Case report:** A 20-year-old female was in hospital for an unrelated collapse from alcohol and benzodiazepine intoxication 3 days prior. She recovered and whilst on the ward she had a vomiting episode with subsequent reduction in conscious state. An urgent review noted that up to 70 × 5 mg tablets were missing from her midodrine supply. The time of ingestion was up to 2 hours prior. Her immediate observations included severe hypertension (blood pressure [BP] 210/100 mmHg), a heart rate of 43–60 beats/min, Glasgow Coma Scale 8/15, spontaneous respirations 20 breaths/min and oxygen saturations >95% on FiO<sub>2</sub> 25%. She was admitted to intensive care for observation but was not intubated. A non-contrast brain computerised tomography (CT) scan did not reveal any intracranial pathology. She was treated with a glyceryl trinitrate patch (5 mg) and observed for a further 36 hours, with subsequent BP reduction to 124/81 mmHg, improvement in conscious state and resolution of vomiting. She was transferred to the psychiatric ward where it was revealed that she had intentionally ingested up to 350 mg of midodrine brought in by her mother, after an emotional trigger whilst watching television. Serum concentrations of midodrine and desglymidodrine were measured with liquid chromatography-mass spectrometry (LC-MS) and confirmed ingestion. **Conclusion:** Midodrine in overdose can potentially cause severe hypertension and reflex bradycardia but given its short half-life, vasodilator agents and supportive care were all that was needed for treatment. It is unclear if central nervous system depression was a direct effect or secondary to the severe hypertension.

## References

- [1] McTavish D, Goa K. Midodrine: a review of its pharmacologic properties and therapeutic use in orthostatic hypotension and secondary hypotensive disorders. *Drugs.* 1989; 38:757–777.
- [2] Perazella M. Efficacy and safety of midodrine in the treatment of dialysis-associated hypotension. *Expert Opin Drug Saf.* 2003;2:37–47.

## 158. Paracetamol toxicity: a survey of awareness in the Eastern province of Saudi Arabia

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**Objective:** Paracetamol is the most widely used antipyretic as it is commonly available over-the-counter. It is generally safe; however, hepatotoxicity may occur in overdose or in patients with risk factors. Paracetamol toxicity accounts for 50% of all cases of acute liver failure (ALF) in the US and carries a 30% mortality.[1] Unintentional toxicity has been estimated to account for 1000 to 2000 cases of ALF, and 100 deaths annually.[2] Poisoning is due to lack of patient awareness and misconceptions regarding the dangers of paracetamol-containing medication leading to misuse. We sought to assess the awareness of the population in the Eastern Province of Saudi Arabia regarding paracetamol. **Methods:** A questionnaire was distributed during an educational campaign for 1 week to individuals over the age of 12, containing multiple choice questions relating to demographic data, level of education, paracetamol usage, side effects, paracetamol-containing products and toxic dose. **Results:** Of the 432 subjects who participated, 217 (50%) were male; 209 (48%) were aged 21–30 years, 118 (27%) 12–20 years and only 11 (2.5%) were aged 51–65 years; 18 (4%) did not give their age. College level education was recorded in 254 (56%) respondents. Paracetamol was used for the relief of headaches (344, 49%) and high temperature (231, 33%). Potential side effects were recorded as damage to internal organs in 243 respondents (48%) and 85 (17%) believed it had no side effects. When asked the amount in a single dose to cause toxicity, 143 (33%) answered 5 tablets, 64 (15%) and 62 (15%) stated 15 and 20 tablets, respectively and 13 (3%) stated 50 tablets. In this population 39% were aware of drugs listed that contained paracetamol, while 9% were not; 66% of respondents were aware that Adol, Panadol Night and Fevadol contained paracetamol, although 13% were not aware that Tempera, Relaxon and Parafon contained paracetamol. In addition, 68% did not recognise that Tylenol contains paracetamol. **Conclusion:** Awareness of paracetamol toxicity in the Eastern Province of Saudi Arabia is below expectations and there is need for more awareness campaigns.

### References

- [1] Ostapowicz GA, Fontana RJ, Schiody FV, et al. Results of a prospective study of acute liver failure at 17 tertiary care centers in the USA. *Ann Intern Med.* 2002;137:945–954.
- [2] Department of Health and Human Services, Food and Drug Administration. Organ-specific warnings: internal analgesic, antipyretic, and antirheumatic drug products for over-the-counter human use; final monograph. Federal Register. 2009;74:19385–19409.

## 159. Appropriate medication administration by medical trainees when treating serotonin syndrome

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**Objective:** Medication safety events are an important cause of morbidity and mortality in healthcare. Despite the frequent prescription of serotonergic medications, medical students and housestaff (HS) at the authors' institution are often unable to identify serotonergic drug interactions during their toxicology rotation. The objective of this study was to determine if senior (4th year) medical students (MS-4) and HS are cognizant of medications that have serotonergic activity that could potentiate serotonin syndrome. **Methods:** A clinical vignette regarding an adolescent male who presents with fulminant serotonin syndrome after abusing dextromethorphan was distributed via email listserv to a MS-4 class and HS across all departments at the authors' institution. Participants were given a list of 10 medications commonly used in the intensive care unit (ICU) and asked to identify which medications were known to increase serotonergic activity and should be avoided in the management of this patient, as well as those medications that are acceptable to administer. Study personnel agreed on five medications in each category, though this distribution was not shared with participants. Chi-squared analyses were used to identify differences in the correct selection of medication by training level (MS-4 versus HS). **Results:** There were 277 respondents to this survey (120 MS-4, 157 HS; overall response rate of 30.3%). Only 2.5% of participants correctly identified all 10 medications, with an overall mean score of 64.9%. There were no differences in mean overall score of medication identification by training level (MS-4 versus HS) or year in training (HS). There was no statistical difference between MS-4s and HS in the proportion that correctly identified all medications that were acceptable to administer ( $p=0.980$ ), as well as the five medications to avoid ( $p=0.169$ ). MS-4s were more likely to identify all five medications that were acceptable to administer than HS (49.2% versus 34.4%;  $p=0.013$ ). HS departments requiring an elective in medical toxicology had a greater overall average score compared to departments not requiring the elective (71.8% versus 63.7%,  $p=0.008$ ). **Conclusion:** In this study, MS-4s and HS often failed to recognize the serotonergic effects of commonly used medications in the ICU, which could result in an adverse drug event. Although training level did not improve overall outcome, HS departments requiring a medical toxicology elective had a statistically significant improvement in overall score. While many factors contribute to ensuring patient safety regarding medication administration, further education is needed for medical trainees regarding medication safety and adverse drug reactions.

## 160. Methadone intoxication treated at an emergency centre in Serbia from 2011 to 2014

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**Objective:** Methadone is a long-acting synthetic opioid as well as a full agonist of  $\mu$  opioid receptors.[1] It is not only used for methadone maintenance treatment (MMT) of opiate addicts but

also in the treatment of cancer pain and chronic pain resulting from other etiologies.[2] Methadone intoxication usually occurs as a result of drug overdose in opiate addicts or accidental poisoning in children and the elderly.[3] The objective of this study was to determine the characteristics of methadone intoxication in patients treated at the Emergency Centre, Clinical Centre of Vojvodina, Serbia. **Methods:** Data were collected from medical records of patients hospitalized for suspicion of opioid intoxication at the Emergency Centre between 2011 and 2014. **Results:** During this time period, there were 278 patients hospitalized for suspicion of opioid intoxication. In 47.0% of them methadone was the main etiological factor. The majority of patients were hospitalized during 2014. Most of them (77.78%) were male. The mean age of patients was  $33.5 \pm 8.0$  years. Analyzing anamnestic data, 37.0% of patients reported that they had taken methadone, while 14.8% were patients receiving MMT. The mean methadone dose was  $154.0 \pm 162.7$  mg. The majority of patients (83.7%) had taken methadone orally. In the toxicological reports of 15.6% patients, only methadone was present; while in others methadone had been taken with other drugs. A small number of patients (4.4%) were admitted to the Intensive Care Unit of the Emergency Centre; one patient died. **Conclusion:** The number of intoxication cases increased during the study period; it is therefore important to advise caution not only when prescribing methadone to patients in MMT but also when treating methadone-intoxicated patients. Particular attention should be paid to the prevention of methadone abuse and its availability on the illicit market.

## References

- [1] Mijatović V, Samojlik I, Ajduković N, et al. Methadone-related deaths – epidemiological, pathohistological, and toxicological traits in 10-year retrospective study in Vojvodina, Serbia. *J Forensic Sci.* 2014;59:1280–1285.
- [2] Mijatović V, Dickov A, Petković S, et al. Safety assessment of low doses of methadone in combination with benzodiazepines in real occasions during methadone maintenance treatment. *Heroin Addict Relat Clin Probl.* 2013;15:29–34.
- [3] Mijatović V, Samojlik I, Petković S, et al. Consequences of cardiac toxicity in patients on low methadone doses during methadone maintenance treatment. *Heroin Addict Relat Clin Probl.* 2015;17:73–78.

## 161. Rhabdomyolysis associated with synephrine and yohimbe containing nutritional supplements and weight lifting

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**Objective:** To report a case of rhabdomyolysis with acute renal injury associated with the use of nutritional supplements to enhance body building. **Case report:** A 22-year-old male in prior good health reported to an emergency department with generalized fatigue, muscle soreness, nausea, anorexia, and dark urine. For the two days prior to arrival, he had supplemented exercise with the nutritional supplement HyperFX Concentrated Energy Formula. The ingredient list stated the product contained caffeine and bitter orange extract (30% synephrine). He also used Mega Men Energy and Metabolism Supplement containing yohimbe. Social history was positive for cigarette smoking, moderate alcohol use and occasional marijuana use. Vital signs on arrival were

temperature  $36.5^{\circ}\text{C}$ , pulse 72/minute, respirations 18/minute, blood pressure 160/86 and oxygen saturation 99% on room air. Mucus membranes were dry. There was no muscle tenderness. No other examination findings were reported. Creatine kinase (CK) was 295,040 U/L and peaked at 791,520 U/L (reference range 32 to 294 U/L). Creatinine peaked at  $386.5 \mu\text{mol/L}$  (reference range 53 to  $106 \mu\text{mol/L}$ ) on hospital day 3. Urine was red with 3+ protein. Treatment with IV hydration with normal saline, urine alkalisation and furosemide resulted in normalization of CK and creatinine, and he recovered without sequelae. **Conclusion:** Sympathomimetic-containing nutritional supplements, when combined with exercise can cause rhabdomyolysis and significant impairment of renal function.[1,2] The HyperFX Concentrated Energy Formula supplement is specifically marketed to be “well-suited to long sessions of aerobic activity or high intensity workouts”.[3] Physicians should obtain a detailed history about supplement use in patients presenting with muscle injury or new renal injury. While association does not establish causation, based on other experiences, workouts augmented by supplements containing sympathomimetics may be associated with health risks and should be used with caution.

## References

- [1] Scroggie DA, Harris M, Sakai L. Rhabdomyolysis associated with nutritional supplement use. *J Clin Rheumatol.* 2000;6:328–332.
- [2] Dehoney S, Wellein M. Rhabdomyolysis associated with the nutritional supplement Hydroxycut. *Am J Health Syst Pharm.* 2009;66:142–148.
- [3] BSN Product Website, 2014; [cited 2015 Nov 2]. <http://www.gobsn.com/product/hperflx.html>

## 162. Diabetic medication enquiries to the New Zealand National Poisons Centre

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**Objective:** To characterize diabetic medication exposures in New Zealand using data reported to the New Zealand Poisons Information Centre. **Methods:** Telephone enquiries involving human exposures to diabetic medications (anti-diabetics and insulin) between January 2005 and December 2014 were retrospectively reviewed. Data on patient age, reason for exposure, substances involved, route of exposure, symptomatology and recommended treatment were collated and assessed. **Results:** Over the study period 81,249 human therapeutic exposure enquiries were received, 634 involving diabetic medications (388 single diabetic medications, 75 multiple diabetic medications, and the remainder involving diabetic medications in combination with other medications). Metformin was the most commonly involved substance (53%), followed by insulin formulations (17%), gliclazide (14%), glipizide (13%) and pioglitazone (1%). Acarbose, exenatide, rosiglitazone and glibenclamide were involved in <1% of cases. Adults accounted for 58% of incidents, with 36% occurring in children <5 years. This is notably different from total pharmaceutical poisonings for the period where 32% involved adults and 57% involved children <5 years. Regarding specific diabetic medications, insulin exposures occurred mainly in adults (93%), while 57% of metformin exposures occurred in adults and 36% in children <5 years. Sulfonylurea incidents were spread 40% in adults and 52% in children <5 years. Poisonings were mainly therapeutic

errors (41%) and child exploratory behavior (39%). Ingestion was the main route of exposure (83%), followed by injections (17%). One incident involved the insufflation of a ground up glipizide tablet. Diabetic medication exposures increased from the beginning of the study period; there were 43 cases in 2005 with a peak of 90 incidents in 2013. Medical referral for monitoring and/or treatment was recommended in 74% of cases. This is considerably higher compared to all pharmaceutical poisonings where only 31% of patients required medical referral. Home observation was recommended in 23% of diabetic poisonings, typically following accidental metformin exposures. Symptoms were reported in 38 of the patients who took hypoglycemic medications only. The most common symptoms were central nervous system depression, dizziness/light-headedness, hypoglycemia and gastrointestinal upset. **Conclusion:** Poisoning exposure to diabetic medications is a fairly infrequent occurrence in New Zealand. However, medical assessment is recommended more frequently, and adults are more commonly involved, compared to other pharmaceutical overdoses. As most cases involved therapeutic errors or child exploratory exposures, secure storage of medications away from children and ensuring the correct medications are given to the correct patient at the correct time could help to reduce the incidence of poisonings.

### 163. Delirium following loperamide overdose: a case report

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**Objective:** Loperamide is an effective oral anti-diarrheal agent in adults and older children. It acts as an agonist at the  $\mu$ -opioid receptor (MOR) but has very low systemic availability and crosses the blood brain barrier (BBB) poorly. Hence, opioid action is usually restricted to the intestinal tract with no central effects. However, bioavailability and central nervous system (CNS) penetration of loperamide may increase in overdose or if other permissive factors are present. We describe a case of agitated delirium during treatment with high dose loperamide. **Case report:** An 80-year-old woman presented with a high-output stoma after sigma resection due to endometrial carcinoma with post-actinic stenosis of the small intestine and sigmoid. The patient was treated with loperamide 30 mg once daily and colestyramine. Her other medication was unremarkable. Despite the already high daily dose, loperamide was increased to 40 mg once daily and colestyramine was stopped. The following day she became somnolent and confused. With antipsychotic therapy and discontinuation of loperamide, somnolence and delirium fully resolved. **Conclusion:** Loperamide is a lipophilic compound that is mostly absorbed in the small intestine. P-glycoprotein (P-gp) efflux and cytochrome P<sub>450</sub> 3A4 metabolism in the intestine and the liver reduce its systemic availability to 0.3%. [1] Loperamide shows highly potent MOR affinity similar to fentanyl, [2] so even modest increases in plasma concentrations could cause central effects. Due to its over-the-counter availability and potential for recreational abuse, loperamide has previously been described as "the poor man's methadone" and is misused in combination with medications which increase its bioavailability. [3] High-throughput stoma increases intestinal transit time, thereby impairing the capacity for loperamide absorption. In this patient, colestyramine had likely further decreased loperamide absorption by unspecific binding in the gut lumen. We propose that the combination of the high dose of loperamide and discontinuation of colestyramine resulted in a sudden and sharp rise in availability, possibly overwhelming

intestinal and BBB P-gp efflux capacities. Clinical management includes withdrawal of drug and symptomatic management. Naloxone can be given as a specific antidote.

### References

- [1] Janssen-Cilag AG Zug, Switzerland. Product Information Imodium Duo<sup>(R)</sup>. 2011; [cited 2015 Nov 4]. Available at: [http://www.imodium.ch/sites/default/files/product/Imodium\\_duo\\_gebrauchsinfo.pdf](http://www.imodium.ch/sites/default/files/product/Imodium_duo_gebrauchsinfo.pdf)
- [2] Chen Z, Davies E, Miller W, et al. Design and synthesis of 4-phenyl piperidine compounds targeting the mu receptor. *Bioorg Med Chem Lett*. 2004;14:5275–5279.
- [3] Dierksen J, Gonsoulin M, Walterscheid JP. Poor man's methadone: A case report of loperamide toxicity. *Am J Forensic Med Pathol*. 2015;36:268–270.

### 164. Accidental intravenous administration of a *Lactobacillus reuteri* preparation in a neonate

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**Objective:** We describe a case of accidental intravenous (IV) dosing of *Lactobacillus reuteri* in a neonate. **Case report:** A male infant born at 38+5 gestational weeks by Cesarean section (3.022 g, Apgar 9/9/10) was transferred to the neonatal care unit at the age of three days because of poor sucking, drowsiness and decreasing weight (–13%). IV benzylpenicillin, netilmycin and aciclovir were started because the symptoms and marginal leucopenia ( $8.9 \times 10^9/L$ ) suggested infection. Blood culture and herpes virus samples were later found to be negative. Enteral nutrition via nasogastric tube was initiated, and resulted in weight increase. At 7 days old the infant still had a nasogastric tube and an IV cannula. A nurse, after administering the IV antimicrobials asked the mother to give Relu Drops<sup>(R)</sup> (*Lactobacillus reuteri*, vegetable oils and colloidal anhydrous silica) to the infant. In error the mother administered the probiotic drops into the IV cannula, but this was not discovered until the evening of the same day, when the infant started to grunt. The IV cannula was immediately removed. The infant seemed otherwise normal, except for tenderness at the infusion site and elevated C-reactive protein (CRP) 44 mg/L. After placement of a new IV cannula and blood culture, penicillin and netilmycin doses were increased. IV paracetamol was used for analgesia. The infant became tachypnoeic, was restless and developed respiratory acidosis (pH 7.27, pCO<sub>2</sub> 7.8 kPa). Therefore nasal continuous positive airway pressure (CPAP) without additional oxygen was initiated. On the first day after the incident (day 2) chest X-ray revealed a large left-sided atelectasis and pneumonia was suspected. CRP peaked at 102 mg/L. In the evening episodes of tremors, rigidity (opisthotonus) and bradycardia (80/min) without hypoxia were observed and he was transferred to a neonatal intensive care unit. G-penicillin was switched to meropenem due to neurologic symptoms (liquor leucocytosis up to  $50 \times 10^6/L$ ) and suspected meningitis. All cultures remained negative and the CRP and the child's clinical state stabilized. Neurological status, brain ultrasound and magnetic resonance

imaging (MRI) were normal and no specific abnormalities were seen on electroencephalogram. Bacteria cultured from the Rela Drops® preparation proved sensitive to netilmycin. Antimicrobial treatment was continued until day 11 and the infant was discharged on day 13 without sequelae. **Conclusion:** Accidental intravenous administration of probiotic drops led to a serious adverse reaction in a neonate. It could not be determined whether symptoms were caused by infection or microemboli or both.

## 165. Severe prolonged tachycardia after massive overdose of paliperidone

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**Objective:** Paliperidone (9-hydroxyrisperidone) is a second generation atypical antipsychotic. The recommended dose for schizophrenia is 6 mg/day. We report a massive paliperidone ingestion demonstrating prolonged significant cardiovascular toxicity, with serum concentrations. **Case report:** A 23-year-old female presented three hours after ingestion of extended release paliperidone 504 mg, quetiapine 400 mg and zopiclone 15 mg. She was drowsy with heart rate 96/min, blood pressure 130/70 mmHg, respiratory rate 14/min and pulse oximetry 98% on room air. Renal function, electrolytes, liver function tests, calcium, magnesium and phosphate were normal. A 12-lead electrocardiogram (ECG) three hours post-ingestion revealed sinus tachycardia (110 beats/min), with normal conduction intervals. Ten hours post-ingestion she was tachycardic on ambulation with a heart rate of 140–180 beats/min, and a resting heart rate of 90–110 beats/min and systolic blood pressure 95 mmHg. Tachycardia developed within seconds of minimal exertion, including small postural changes while supine. One liter of intravenous crystalloids was administered and blood pressure normalized. Serial ECGs showed sinus tachycardia (up to 184 beats/min) with absolute QT interval of 320 msec (which remained constant). She was admitted to the coronary care unit for monitoring and bed rest. Intravenous magnesium and potassium (low normal serum potassium) were administered. Tachycardia persisted for 72 hours peaking at 190 beats/min on any exertion 36–40 hours post-overdose. ECG on discharge showed sinus rhythm of 100 beats/min, PR interval 100 msec, and an absolute QT interval of 320 msec. We were unable to obtain a transthoracic echocardiogram to assess cardiac function. Serum paliperidone concentrations 4 and 40 hours post-ingestion were 29 ng/mL and 883 ng/mL respectively. A mean plasma concentration of 10.7 ng/mL is reported following daily 3 mg dosing.[1] Quetiapine was not detected in serum at 40 hours post-ingestion. **Conclusion:** Paliperidone in overdose can cause prolonged cardiovascular dysfunction characterised by resting sinus tachycardia with intermittent episodes of posture-evoked extreme tachycardia. Its availability as an extended release preparation results in high blood concentrations and effects that can persist for several days. This case is the largest recorded paliperidone overdose, with confirmatory serum concentrations. We recommend a period of prolonged cardiac monitoring and minimal exertion in patients with significant overdose. Prescribers should be aware of the potential for significant prolonged paliperidone toxicity when taken in overdose.

## Reference

- [1] Boom S, Talluri K, Janssens L, et al. Single and multiple-dose pharmacokinetics and dose proportionality of the psychotropic agent paliperidone extended release. *J Clin Pharmacol.* 2009;49:1318–1330.

## 166. Overdoses of ropinirole reported to the UK National Poisons Information Service

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**Objective:** Ropinirole is a dopamine D2/D3 receptor agonist for the treatment of Parkinson's disease and restless legs syndrome. As there is little information on overdose this study was carried out to review UK National Poisons Information Service (NPIS) enquiries. **Methods:** Information was extracted from telephone enquiries received by the NPIS and recorded on the UK Poisons Information Database from 1 January 2008 to 31 August 2015. **Results:** There were 113 enquiries concerning 104 exposures (2 tablet identification requests and 7 duplicate calls). Where age was known the mean was 59.7 years (median 63; range 1–100). There were 43 females and 58 males, remainder unknown. Eight enquiries concerned children (1–3 years) who had taken 1–8 mg. One vomited, one was described as "sleepy and grumpy", in one features were unknown and 5 were asymptomatic. For the 96 adults (mean age 65 years; 41 females, 53 males, remainder unknown), 11 were described as deliberate overdoses. Two patients had taken ropinirole alone (24.5 mg and 58 mg) and both were asymptomatic (5 hours and 30 minutes post-ingestion). Of the other 9, one had a poisons severity score of 2 (PSS2) [1] (29-year-old female patient with Parkinson's disease who had taken 112 mg ropinirole and 10 mg rasagiline, and had dyskinesia, agitation and hallucinations) and one PSS3 (33-year-old male with a history of ingesting a variety of drugs including a beta-blocker, presented with coma, twitching, mydriasis, tachycardia and hallucinations, developed respiratory arrest and convulsions but recovered and then claimed only to have taken alcohol). The remaining patients scored PSS0 or 1. The non-intentional ingestions (85) were therapeutic errors (65), accidental overdoses (12), adverse reactions (3), or circumstances unknown (5). In the 41 cases where ropinirole was taken alone, no features greater than PSS1 were reported and 23 were asymptomatic. Features reported were (frequency >1): vomiting (7), nausea (6), dizziness (4) and somnolence (2). Of the adverse effects reported during therapeutic use, the following were reported in this series: abdominal pain (1), confusion (3), dizziness (6), hallucinations (4), hypotension (1), nausea (6) and vomiting (6). **Conclusion:** Most poisons centre referrals concerning ropinirole were therapeutic errors or accidental overdoses. Most patients who take excess ropinirole accidentally do not have serious effects and features reported are similar to those found in therapeutic use.



## Reference

- [1] Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998;36:205–213.

## 167. Safety of antipsychotic drugs: a 16-year review

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**Objective:** Evaluation of the safety profile of traditional and atypical antipsychotics in overdose, causes of intoxications and demographic indicators. **Methods:** Intoxications were analysed on the basis of data gathered from telephone consultations and medical reports forwarded to the National Toxicological Information Centre (NTIC) in Bratislava from the whole of Slovakia during the period 1999–2014. All cases involving the non-prescribed use or overdose of antipsychotics were reviewed. Only coingestion of ethanol was accepted. The severity of poisoning was classified in accordance with the Poisoning Severity Score. **Results:** Over the 16-year period 2339 antipsychotic exposures were the subject of enquiries to the NTIC of which 1150 involved single agent antipsychotic ingestions. We registered 642 (55.8%) atypical antipsychotic overdoses and 508 (44.2%) incidents with first generation antipsychotics. Since 1999 there has been a 3.5 fold increase in antipsychotic overdoses. The median age of patients was 31 years (1 to 92 years), 53.1% of cases involved females. Suicidal intoxications were more frequent (80.3%) and had a more serious clinical course. Accidental poisonings (16.6%) occurred mostly in children under 6 years of age. Risperidone, quetiapine and tiapride made up most of the atypical antipsychotic overdoses. Levomepromazine and chlorprothixene were the most frequently involved in the traditional antipsychotic poisonings. Clinical symptoms of intoxication were manifested in 920 patients (79.9%) of the observed group. We registered just 152 cases (13.2%) in which no symptoms were manifested after the non-prescribed use or overdose. The most frequent (717 cases, 62.3%) were minor symptoms (sleepiness, dizziness, gastrointestinal distress, mild extrapyramidal symptoms, hypotension) that subsided in 24 hours. In 152 (13.2%) patients we observed symptoms of moderate and in 49 (4.2%) patients symptoms of severe intoxication. Severe intoxications in 2 (0.17%) patients overdosed with clozapine resulted in death. In total 788 (68.5%) patients were hospitalised. The median length of hospital stay was 2 days (1–28 days). **Conclusion:** Atypical antipsychotic overdoses dramatically increased over the 16-year period, together with their rising prescription. During this time, there was no decline in severity or the length of hospital stay, despite the reduction in first generation antipsychotic overdoses. According to our findings, there is no significant difference in safety profile between atypical and traditional antipsychotics.

## 168. Severe taxane skin reaction due to a drug interaction with amiodarone: a case report

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**Objective:** Paclitaxel and docetaxel are taxanes that are used in chemotherapy of several solid tumors. They are eliminated from the cell by P-glycoprotein (P-gp) and inactivated by CYP 3A4 (docetaxel, paclitaxel) and CYP 2C8 (paclitaxel). We report a case of severe taxane toxicity due to co-medication with the antiarrhythmic drug amiodarone. **Case report:** A 77-year-old woman with invasive ductal breast cancer was referred to our hospital with blistering of the skin, inability to swallow solids or liquids, and dehydration. She was undergoing chemotherapy as an adjunct to surgery. Her medication included amiodarone which she was taking for her “palpitations”. During the first four cycles of outpatient paclitaxel therapy she developed increasing abdominal discomfort and skin lesions. Therapy was switched to docetaxel because of paclitaxel’s known potential for skin toxicity, however symptoms worsened, mucositis ensued, and chemotherapy was discontinued after only one cycle of docetaxel. Over the next days, however, symptoms progressed, eventually making oral intake impossible. On admission, we began intravenous hydration, symptomatic treatment of the skin reaction, and placed a nasogastric tube to allow for administration of medication and nutrition. Analysis of two routine blood samples taken 9 and 10 days after docetaxel revealed serum concentrations of 4.73 and 4.09 ng/mL, respectively, corresponding to a severely prolonged terminal half-life of 114 hours (reference 11.1 hours). Paclitaxel was also present in these blood samples (20 and 21 days after the last administration, respectively), but concentrations were below the validated lower limit of detection.[1] Under normal conditions, paclitaxel should not be detectable 11 days after the last administration. The patient was discharged two weeks later with near resolution of the skin and mucosal lesions. There were no recurrences of dermatological or gastrointestinal toxicity on follow up. **Conclusion:** Amiodarone is a strong P-gp inhibitor and a moderate CYP 3A4 inhibitor. There is evidence for CYP 2C8 inhibition.[2] We show the inhibitory effects of amiodarone on taxane clearance. We also suggest caution when combining other CYP 2C8 inhibitors with paclitaxel.

## References

- [1] Hendriks JJ, Rosing H, Schinkel AH, et al. Combined quantification of paclitaxel, docetaxel and ritonavir in human feces and urine using LC-MS/MS. *Biomed Chromatogr.* 2014;28:302–310.
- [2] Polasek TM, Elliot DJ, Lewis BC, et al. Mechanism-based inactivation of human cytochrome P4502C8 by drugs *in vitro*. *J Pharmacol Exp Ther.* 2004;311:996–1007.

## 169. Acute iatrogenic parenteral vancomycin overdose and associated nephrotoxicity: a case report

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**Objective:** Vancomycin-associated nephrotoxicity, first reported in 1958, was initially thought to be due to the presence of impurities. Newer preparations are devoid of such impurities, yet nephrotoxicity still occurs. The majority of cases involve treatment with vancomycin for >48 hours, high trough concentrations, pre-existing chronic kidney disease, or concurrent use of other nephrotoxic drugs. We present the first reported case of acute iatrogenic vancomycin-associated nephrotoxicity occurring within hours of drug administration. **Case report:** A 13-year-old, 60 kg girl with scoliosis was admitted to the pediatric intensive care unit after undergoing an uncomplicated spinal fusion. Only acetaminophen 800 mg IV was prescribed. On post-operative day one she received a dose and immediately developed flushing without shortness of breath or urticaria. Vital signs were blood pressure 112/59 mmHg, heart rate 130/minute, respiratory rate 27/minute and temperature 38.9 °C. Diphenhydramine IV and a fluid bolus were administered. Thirty minutes later, pharmacy called reporting a dispensing error; the patient had received 8 g vancomycin. A serum vancomycin concentration one hour after administration was 93 µmol/L (139 µg/mL). Two hours later her creatinine (Cr) was 89 µmol/L (1.01 mg/dL), a 100% increase from her baseline 44 µmol/L (0.5 mg/dL). Five hours later, her Cr was 121 µmol/L (1.37 mg/dL) and vancomycin concentration was 96 µmol/L (144 µg/mL). Nephrology performed hemodialysis (HD) for 5 hours. Post-dialysis, her Cr was 17 µmol/L (0.2 mg/dL) and vancomycin was undetectable. However, two hours later, her Cr and vancomycin concentration increased to 165 µmol/L (1.87 mg/dL) and 42 µmol/L (63 µg/mL), respectively. Her urine output decreased to 0.7 ml/kg/h. A second session of HD was performed 13 hours after the initial error. Over the next 24 hours, Cr continued to rise, but her vancomycin concentration declined without further HD. On day 8, Cr returned to baseline and she was discharged on day 9 stable with mild hypertension. **Conclusion:** The mechanism for acute vancomycin-associated nephrotoxicity remains unclear. Proposed mechanisms include oxidative injury and ischemia leading to tubulo-interstitial damage and mitochondrial dysfunction within proximal renal tubule cells. The etiology of nephrotoxicity in our patient is unknown, however the single drug exposure and close temporal relationship suggests vancomycin played a significant role. This case suggests a significant increase in serum Cr may occur following a single acute parenteral vancomycin overdose. Further research is needed to determine if this rise in Cr is due to laboratory interference, increased Cr production, decreased Cr secretion, or acute tubular injury.

## 170. What are the causes of and how to prevent medication errors by laypersons?

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**Objective:** The causes of unintentional medication errors by lay persons are rarely studied. The identification of the frequency, sources, reasons and consequences could help to reduce their overall rate. **Methods:** Records of medication error enquiries in 2013–2014 were extracted from the electronic database of the Toxicological Information Centre (TIC) and following variables were reviewed: drug class, dosage form, dose, age of the subject, cause of the error, time interval from ingestion to the call, symptoms, prognosis evaluation at the time of the call and first aid recommended. **Results:** Overall 1354 calls met the inclusion criteria, including central nervous system (CNS) drugs (23.6%), respiratory system drugs (18.5%) and gastrointestinal drugs (16.2%) were the most common drug classes involved in the medication errors. Symptoms at the time of the call were mostly absent (73.0%), minor (18.3%), irrelevant/not related (6.5%), moderate (1.7%), and rarely severe (0.5%). The ingested dose, as evaluated by TIC toxicologists was mostly mild (42.6%), less frequently low/therapeutic (35.1%), causing only mild gastrointestinal discomfort/irritation (12.8%), toxic (9.4%), or lethal (0.1%) effects. Most patients were in the youngest age subgroup 0–5 years (46%), followed by 20–59 years (29%), 6–12 years (11%), ≥60 years (9%) and 13–19 years (5%). Most errors were caused by parents (59.0%), less by patients themselves (35.9%). The recommendations of the TIC included oral fluids (16%) or charcoal (8%) administration. Other measures (total 5%) were less frequent, such as superficial decontamination, vomiting induction, gastric lavage, symptomatic treatment or administration of antidotes (N-acetylcysteine or digitalis antidote in the most severe cases). The most frequent reasons for the errors involved leaflet misinterpretation and/or mistaken dose (53.6%), mixing up medications (19.2%), attempt to reduce pain with repeated dose (6.4%), confusion in psychiatric/elderly patients (2.7%), wrong route of administration (2.2%), accident with the closure of the bottle and other (9%) or unknown cause (6.9%). **Conclusion:** The high proportion of children among the patients is worrying and small children are rather surprisingly the most vulnerable group. The reason may be that children's dosages vary by weight. In addition, many drugs come in several concentrations and a proper dose adjustment is more difficult. Most overdoses could be prevented by safer labelling, proper cap closures for liquid products and medication reconciliation by both physicians and pharmacists teaching patients how to use medicines properly. **Acknowledgements:** Charles University projects P25/1LF/2 and P28/1LF/6.

## 171. A case of flecainide overdose responding to lipid emulsion therapy

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**Objective:** Lipid emulsion therapy is considered for cardiotoxic drug overdoses unresponsive to other therapies.[1] Two cases report flecainide overdoses responding to fat emulsion therapy.[2,3] We report a similar case. **Case report:** A 69-year-old man with history of depression, atrial fibrillation, and restless leg syndrome informed his spouse that he had ingested 1 g of flecainide, 12 mg of clonazepam, and 1 mg of ropinirole. She drove him to the hospital. On arrival, he complained of dyspnea and dry cough, but had no other complaints. Initial vital signs one hour after ingestion were pulse 75/minute, respiratory rate 16/minute, blood pressure (BP) 119/62 mmHg, and oxygen saturation 98% on room

air. Initial electrocardiogram 70 minutes after ingestion demonstrated a broad complex irregular tracing with heart rate of 76/minute, QRS duration 268 msec, and QTc interval 644 msec. At 79 minutes after ingestion his BP fell to 66/29 mmHg. He was given a bolus of 150 mEq of sodium bicarbonate followed by a continuous infusion, with no improvement in hypotension or shortening of QRS duration. Coughing, rales, and hypoxia developed two hours after ingestion. Chest roentgenogram confirmed pulmonary edema. Rapid sequence intubation was performed without incident. Central and arterial lines were placed. A 135 mL bolus of a 20% lipid emulsion therapy was followed by a continuous infusion of 1350 mL over two hours. BP rose to 100/66 mmHg at 2.5 hours after ingestion, then to 152/94 mmHg. There were no further hypotensive episodes. The patient was transferred to the cardiac intensive care unit (CICU). His hospital course was complicated by atrial fibrillation requiring medication adjustment and pulmonary edema requiring diuresis. He made an uneventful recovery and was transferred to the psychiatric service two weeks after admission. **Conclusion:** In this case of flecainide overdose, there was a rapid reversal of hypotension after lipid emulsion therapy was instituted after sodium bicarbonate infusion was ineffective.

## References

- [1] American College of Medical Toxicology: ACMT position statement: interim guidance for the use of lipid resuscitation therapy. *J Med Toxicol.* 2011;7:81–82.
- [2] Moussot PE, Marhar F, Minville V, et al. Use of intravenous lipid 20% emulsion for the treatment of a voluntary intoxication of flecainide with refractory shock. *Clin Toxicol (Phila).* 2011;49:514.
- [3] Sivalingam SK, Gadiraju VT, Hariharan MV, et al. Flecainide toxicity – treatment with intravenous fat emulsion and extra corporeal life support. *Acute Card Care.* 2013;15:90–92.

## 172. Paracetamol overdose in Slovenia

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**Objective:** The incidence of paracetamol overdose and paracetamol-induced liver failure varies widely across Europe and the US. In Slovenia paracetamol is an over-the-counter drug. However, it can be bought only in pharmacies with a limited amount of paracetamol in these products. Maximum pack size is 20 tablets in blister packs and up to three packs can be supplied in one transaction. The aim of the study was to evaluate epidemiology of paracetamol overdose in Ljubljana, Slovenia. **Methods:** In this retrospective study we analysed the epidemiology and clinical presentation of adult patients poisoned with paracetamol who were treated in the University Medical Center, Ljubljana (UMCL), the primary city hospital in the capital, serving a population of 600,000, in the past 25 years. **Results:** In total 90 adult patients with paracetamol overdose were hospitalized in UMCL during the past 25 years. The overall incidence of paracetamol overdose was 0.6/100,000 population in this period. The number of paracetamol overdosed patients steadily increased from three patients in 1990 (0.5/100,000) to nine patients in 2014 (1.5/100,000). The mean age of the study cohort was 34 years (range 16–88 years). There were 29 women and 61 men. Of the 90 patients, 78 ingested paracetamol with suicidal intent and 12 paracetamol overdoses occurred by mistake. The ingested dose of paracetamol was known in 71 patient and 56 of them ingested a toxic dose of paracetamol. Nevertheless, a toxic serum concentration was detected in

17 patients only; of these 14 patients ingested paracetamol in a suicide attempt. Overall 40 patients were treated with acetylcysteine and 6 patients developed acute liver failure. No case resulted in liver transplantation or death. **Conclusion:** In Slovenia the incidence of inpatient admissions due to paracetamol overdose is about 10-times lower than in the US.[1] The main reason may be that only pharmacies are allowed to sell paracetamol and a pharmacist must make or supervise the sale. Patients are asked about other medical conditions and other medicines they are taking. So, misunderstanding of the active ingredient is uncommon. Patients can obtain only up to three packs in one transaction and maximum pack size is 20 tablets. In addition, tablets are packaged in blister packs which probably reduce the risk of deliberate ingestion of a larger number of tablets at once.

## Reference

- [1] Altyar A, Kordi L, Skrepnek G. Clinical and economic characteristics of emergency department visits due to acetaminophen toxicity in the USA. *BMJ Open.* 2015;5:e007368.

## 173. Supplementation of vitamin D can be hazardous when exaggerated: a case report

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**Objective:** Vitamin D supplements have become popular and can be purchased easily over the counter in diverse formulations and dosages. They are also marketed on the Internet as a cure for various conditions like depression, tiredness and strengthening of the immune system. We present a case of severe vitamin D poisoning with persistent hypercalcemia and renal failure after repeated intake of colecalciferol intended for horses. **Case report:** A 21-year-old man with Asperger's syndrome presented at the emergency department with severe headache, photophobia, nausea and vomiting after a night of computer gaming. He was previously healthy and denied all kinds of substance intake. Initial suspicion of subarachnoid hemorrhage was excluded with brain computerised tomography (CT) scan and lumbar puncture with normal results. Incidental findings of severe hypercalcemia of 3.64 mmol/L (ionized 1.87) and renal failure with creatinine 153 mmol/L were noted. Extended sampling showed an extremely low concentration of parathyroid hormone (<0.3 pmol/L), and a high 25(OH)-vitamin D, concentration (>350 nmol/L). Treatment was started with intravenous fluids and steroids. Calcitonin was given for 3 days and on day 3 he was given denosumab. Steroid treatment continued for 3 weeks and was then slowly weaned. He developed atrial fibrillation (probably due to treatment with extremely large volumes of fluids) which resolved with diuretics. The high calcium concentration persisted for 2 weeks and continued treatment with large volumes of fluids was necessary to keep calcium at an acceptable concentration. After 3 weeks in hospital the calcium concentration and renal function normalized but the 25(OH)-vitamin D was still 1050 nmol/L and the 1,25(OH)<sub>2</sub>-vitamin D 391 pmol/L. After confrontation, the patient finally admitted two months daily intake of spoonful of an animal product containing 500 000 IU/g vitamin D3 for revitalizing purposes. **Conclusion:** There is ongoing debate on vitamin D supplementation. Fairly high doses are considered safe but the toxic upper

limit is unknown. There is also a difference in tolerated dose in acute poisoning and cumulative exposure. There are previous case reports of severe vitamin D toxicity, but more data needs to be collected regarding toxic doses.[1] There is also a need for easily accessible information on the subject to the general public to avoid hazardous intake.

## Reference

- [1] Vogjazi MG, Jacobsen-Dickman E, Deboer MD, et al. Vitamin D supplementation and risk of toxicity in pediatrics: a review of current literature. *J Clin Endocrinol Metab.* 2014;99:1132–1141.

## 174. QT prolongation after accidental tamoxifen ingestion in a 5-year-old child

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**Objective:** Five percent of all hospital admissions in Europe are caused by adverse drug reactions (ADRs) which are the fifth cause of death in hospital.[1] Therapeutic errors account for 18.7–56% of all ADRs.[2] Tamoxifen is a nonsteroidal antiestrogen that antagonizes estrogen receptors in breast cancer cells thereby preventing their growth.[3] Although tamoxifen overdose is extremely rare, neurotoxicity and prolonged QT interval are described as side effects and the drug is not labeled for pediatric use. **Case report:** Tamoxifen citrate (20 mg) was accidentally administered to a 5-year-old child instead of a leukotriene receptor antagonist used for the maintenance treatment of asthma. After consulting the Poison Center of Florence Careggi University Hospital, the child was admitted to the Emergency Room of Siena Hospital. On arrival, electrocardiogram (ECG) was performed and activated charcoal was administered. Intravenous fluid therapy with saline was started and considering tamoxifen's long half-life (5–7 days), continuous ECG recording was performed. QTc prolongation was observed 9 and 47 hours after ingestion (0.47 s and 0.46 s, respectively). No other symptoms were reported. The child remained in hospital for five days and was discharged after QTc normalization. **Conclusion:** In this case, a single dose of tamoxifen caused the development of QTc prolongation in a pediatric patient. Unintentional therapeutic errors are frequent and can cause severe ADRs and patient hospitalization. The American Association of Poison Control Centers reported that medication errors continue to be a source of preventable injury with increasing incidence across the out-of-hospital population.[4] In 2014, the Poison Center of Florence received 4331 calls and 188 (4.3%) were related to therapeutic errors. Safe and appropriate drug use, risk reduction and error prevention must be promoted.

## References

- [1] Commission Staff Working Document accompanying document to the Proposal for a Regulation of the European Parliament and of The Council amending, as regards pharmacovigilance of medicinal products for human use, dated 10 December 2008; [cited 2015 Nov 26]. Available at: [http://ec.europa.eu/health/files/pharmacos/pharmpack\\_12\\_2008/pharmacovigilance-ia-vol2\\_en.pdf](http://ec.europa.eu/health/files/pharmacos/pharmpack_12_2008/pharmacovigilance-ia-vol2_en.pdf)
- [2] Medication Errors Workshop 28 February – 1 March 2013 Report European Medicines Agency, London, UK; [cited 2015 Nov 26]. Available at: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Report/2013/05/WC500143163.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/05/WC500143163.pdf)
- [3] Product Information: Nolvadex oral tablet. AstraZeneca Pharmaceuticals LP, Wilmington, Delaware, 2004; [cited 2015 Nov 26]. Available at: [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2005/17970s053lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2005/17970s053lbl.pdf)
- [4] Brophy TJ, Spiller HA, Casavant MJ, et al. Medication errors reported to U.S. Poison Control Centers, 2000–2012. *Clin Toxicol (Phila).* 2014;52:880–888.

## 175. Use of octreotide as a novel treatment for insulin overdose in a non-diabetic patient

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**Objective:** Insulin overdose in a non-diabetic patient is uncommon and often difficult to treat. Standard treatment consists of administration of large amounts of intravenous glucose. Diabetic patients who overdose on insulin are relatively easy to manage as blood glucose levels (BGLs) increase once exogenous insulin is eliminated. In contrast, non-diabetics with insulin overdose are still able to produce endogenous insulin, making titration of glucose problematic and the end point of management with glucose difficult to determine. We describe two cases of insulin overdose in non-diabetics where octreotide was used in the second to inhibit endogenous insulin. **Case report:** Case 1: A 28-year-old non-diabetic female presented after injecting 5000 U of 30% neutral insulin/70% isophane insulin into multiple subcutaneous sites on her abdomen. Her initial BGL was 2.6 mmol/L and she was drowsy and diaphoretic. After 50 mL of 50% glucose intravenously her BGL increased to 5.9 mmol/L. Glucose 50% was commenced as an infusion and she received 600 g over 9.5 hours to maintain her BGL >4 mmol/L. On Day 4 the infusion rate was halved with no change in BGL, and then ceased. Following this her BGL increased to >10 mmol/L and then normalised. On admission her insulin was 2769 mU/L and C-peptide 0.7 mcg/L. On day 5 insulin was 29.3 mU/L and C-peptide 3.3 mcg/L. Case 2: A 17-year-old female presented on multiple occasions following large overdoses of combinations of short- and intermediate-acting insulin with hypoglycaemia and undetectable C-peptide concentrations. On the first admission BGLs were erratic and the rates of glucose infusions were difficult to predict. On subsequent admissions octreotide was commenced at 25 U/h with the glucose infusion. Glucose was titrated to maintain the BGL between 4 and 12 mmol/L. In each case an increasing BGL led to the glucose being decreased and subsequently ceased. Octreotide was ceased once glucose was no longer required. **Conclusion:** These cases demonstrate that non-diabetic insulin overdoses are difficult to manage and the body's ability to maintain euglycaemia makes it impossible to determine when glucose treatment can be weaned

and ceased. The series of admissions in the second patient demonstrates that the administration of octreotide removes the effect of endogenous insulin secretion on BGL. This makes it easier to determine when to stop glucose treatment.

## 176. Erroneous intravenous injections

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**Objective:** Erroneous intravenous injection of the wrong drug or of drugs not intended for intravenous use is a rare event. Poison centers are sometimes asked to perform a risk evaluation of such events. We present an overview of calls to the Belgian Poison Centre received over a 10 year period. **Methods:** A search of the Poison Centre data of the last ten years (2005–2014) was undertaken together with a search of the drugs involved. **Results:** Overall there were 130 calls for advice concerning erroneous intravenous injections. This accounted for 0.025% of all calls. There were 74 calls concerning adults, 52 children, 3 dogs and 1 cat. Drugs not intended for intravenous use (mostly oral dosage forms) were involved in 111 cases and 19 cases concerned administration of the wrong intravenous drug. The most frequently encountered drugs were promethazine ( $n=9$ ), ranitidine ( $n=7$ ), methylprednisolone ( $n=6$ ), amoxicillin ± clavulanate ( $n=6$ ), tranexamic acid ( $n=4$ ), lidocaine ( $n=4$ ), paracetamol ( $n=4$ ), olanzapine ( $n=3$ ) and ceftriaxone ( $n=3$ ). Follow up was available for 28 of the 130 injections. The severity of poisoning was none ( $n=17$ ), minor ( $n=7$ ), moderate ( $n=2$ ) and major ( $n=2$ ). The first case with major symptoms was a child of 2 years who received amoxicillin/clavulanate syrup intravenously and developed hypotensive shock with blood pressure 50/30 mmHg. The children recovered with symptomatic treatment. The second case with major symptoms was a 71-year-old man who received vitamin D intravenously. He developed chest pain, dyspnoea, cyanosis and hypotension. He was treated symptomatically and had no more symptoms the next day. As the vitamin D product contained arachis oil a thoracic scan was performed but no emboli were visible. There were no lethal cases. **Conclusion:** Problems which can be encountered with erroneous intravenous injections are a rapid rise of serum concentrations of the involved drug, effects of excipients/drug additives not intended for intravenous use, oil-based medication (fat emboli), suspension (formation of micro emboli) and infection risk. Suitable animal data or comparable case reports are generally not available. This makes risk evaluation difficult. For 70 of the 84 different drugs involved we could find no comparable cases in the literature. Although a rare event, erroneous intravenous injections can have serious consequences. To help Poison Centres to provide quick and adequate advice, sharing of experience in an international database would be a welcome tool for poison control centers.

## 177. Analysis of homeopathic product exposures reported to US Poison Centers

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**Objective:** Homeopathic product sales have increased in the US and European Union.[1,2] Despite their popularity and the general belief in their safety, the US Food and Drug Administration raised questions about homeopathic product regulation and about data sources available to understand homeopathic product safety. This analysis aims to describe homeopathic product exposures reported to US poison centers (PCs) and to discuss how PC data can be used to understand safety concerns related to homeopathic products. **Methods:** The National Poison Data System (NPDS) of the American Association of Poison Control Centers was searched from 2005–2014 for all human exposures to homeopathic products. Age, gender, exposure reason, level of care, and medical outcome variables were analyzed using descriptive statistics. **Results:** In total 101,851 homeopathic product exposures were reported from 2005–2014. Most exposures involved children <12 years old (92%), with children <4 years old representing (83%) of all exposures. Unintentional general exposure reasons were most common (86%; the exposure reason most commonly associated with accidental unsupervised ingestions [AUIs]). Most exposures followed to a known medical outcome resulted in no effect or an unrelated effect (86%) and were managed outside a healthcare facility (HCF; 91%). A medical outcome of major or moderate effect was recorded in 0.9% of exposures. Five deaths were reported, but homeopathic products were determined not to be contributory or responsible for the outcome in any of these cases. **Conclusion:** As reported to US PCs, homeopathic products are relatively safe, with most exposures managed outside a HCF (92%) and few involving major or moderate effect (0.9%). Comparing homeopathic product and all pharmaceutical exposures reported to US PCs in 2013, pharmaceutical exposures involved more management in a HCF (30% versus 8%) and more major or moderate effect (7% versus 0.9%).[3] Safety efforts should target pediatric unintentional exposures, as most homeopathic product exposures involved AUIs (86%). Understanding characteristics and outcomes of PC exposures is useful in evaluating product safety trends.

## References

- [1] Nutrition Business Journal. Supplement Business Report 2015; [cited 2015 Nov 26]. Available at: <http://newhope360.com/nbj-2015-supplement-business-report> [10.18374/JIMS-15-3.6]
- [2] European Coalition on Homeopathic and Anthroposophic Medicinal Products E.E.I.G. Homeopathic and Anthroposophic Medicine in Europe. Facts and Figures. 2007; [cited 2015 Nov 26]. Available at: [http://www.echamp.eu/fileadmin/user\\_upload/Brochures/ECHAMP-FlyerF\\_F-4p.pdf](http://www.echamp.eu/fileadmin/user_upload/Brochures/ECHAMP-FlyerF_F-4p.pdf)
- [3] Mowry JB, Spyker DA, Cantilena LR Jr, et al. 2013 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 31st Annual Report. Clin Toxicol (Phila). 2014;52:1032–1283.

## 178. Vincristine fatality after accidental intrathecal administration: analytical and therapeutic challenges

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**Objective:** Intravenous administration of vincristine (VCR) is used in the treatment of several malignancies. Inadvertent intrathecal administration produces ascending paralysis and severe neurotoxicity that can progress to respiratory failure and coma. This medical error is usually fatal, and occurs when VCR is confused with other drugs, mainly methotrexate. No specific treatment has been reported. Immediate cerebrospinal fluid (CSF) drainage and early irrigation may be useful to prolong survival.[1] We report a fatal case of analytically confirmed intrathecal accidental administration of vincristine. **Case report:** VCR (1.3 mg) was accidentally administered intrathecally instead of methotrexate to a 56-year-old male patient with a positive history for leukemia, hepatitis C virus (HCV) and human immunodeficiency virus (HIV). Considering the severe potential toxicity and although the patient was asymptomatic, an early (4 hours later) continuous external ventricular drainage (EVD) was placed and continued for 5 days. Cerebrospinal fluid, blood and urine samples were stored during EVD procedures. Pyridoxine, folinic acid and cyanocobalamin were also administered. The clinical condition worsened progressively and he developed paralysis (with level at T10) at day 8, respiratory failure and adult respiratory distress syndrome (ARDS) requiring respiratory support. The patient died on day 31. To guide the invasive treatment (EVD), an analytical method for VCR determination was promptly developed and quantitative determinations were performed using ultrahigh performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) (Acquity-TQD, Waters). VCR concentrations in CSF were 4.9 mg/L (before EVD) and 0.01 mg/L (11 hours after EVD started). VCR was undetectable from the second day, and was negative (limit of detection 0.004 mg/L) in all serum and urine samples. **Conclusion:** Accidental intrathecal administration of vincristine is a clinical emergency with dramatic evolution. Urgent and continuous EVD (for at least 48 hours) decreases the concentration of VCR in CSF and seems to be sufficient to significantly and rapidly reduce the VCR concentration, however, in our case this was not sufficient to reduce neurotoxicity that occurred one week later. The patient's clinical condition worsened and the severe pre-existing diseases may have contributed. The method in UPLC-MS/MS is suitable for the rapid detection of VCR in CSF and essential to guide the duration of continuous EVD.

## Reference

- [1] Pongudom S, Chinthamittr Y. Inadvertent intrathecal vincristine administration: report of a fatal case despite cerebrospinal fluid lavage and a review of the literature. *J Med Assoc Thai.* 2011;94:S258–S263.

## 179. Convulsions associated with analytically confirmed phenibut ingestion

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**Objective:** Phenibut is a neuropsychotropic drug structurally similar to  $\gamma$ -aminobutyric acid (GABA) used for its anxiolytic and cognition enhancing effects. We report a case of analytically confirmed phenibut ingestion associated with toxicity including convulsions. **Case report:** A 71-year-old male with a history of

myalgic encephalopathy and depression was admitted with vomiting, agitation, hallucinations and reduced conscious level (Glasgow Coma Scale (GCS) 10/15). Despite administration of lorazepam 1 mg intravenously for agitation, he developed a generalised tonic-clonic seizure terminated with a further 3 mg of intravenous lorazepam. He remained haemodynamically stable with a blood pressure of 103/52 mmHg and heart rate of 67 bpm. He had a 2 day intensive care unit admission for observation following seizures and reduced GCS without requiring circulatory or ventilation support. His confusion slowly improved with normalisation of his conscious level over 48 hours. Initial hyponatraemia (123 mmol/L) self-corrected over the first 24 hours; other blood tests were unremarkable. A 12-lead electrocardiogram (ECG) following the seizure revealed a borderline prolonged QTc (475 ms at 75 bpm). The following day T wave inversion in V3 and QTc of 509 ms at 87 bpm were noted; these normalised by discharge. On recovery he confirmed ingesting a "teaspoonful" of phenibut to improve his motivation and energy; despite "online instructions" recommending taking a "1/4 spoonful". His regular medications included gabapentin for back pain (started 6 years previously), which he denied taking in excess. Phenibut was identified from a serum sample by liquid chromatography-mass spectrometry. **Conclusion:** Limited information has been published in English on adverse effects following therapeutic dose or overdose of phenibut. Tonic-clonic seizures have been described in presumed phenibut use without analytical confirmation,[1] whereas analytically confirmed recreational use of phenibut has been associated with fluctuating levels of consciousness, agitation, delirium, somnolence, dystonia and dilated pupils; with some cases requiring intubation and critical care admission.[2,3] This case indicates that phenibut toxicity may be associated with convulsions, but further information on the clinical features of phenibut toxicity is required.

## References

- [1] Marraffa JM, Nacca NE, Stork CM, et al. Phenibut: One poison center's experience. *Clin Toxicol (Phila).* 2014;52:736–737.  
 [2] Wong A, Little M, Caldicott D, et al. Analytically confirmed recreational use of phenibut ( $\beta$ -phenyl- $\gamma$ -aminobutyric acid) bought over the Internet. *Clin Toxicol (Phila).* 2015;53:783–784.  
 [3] Downes MA, Berling IL, Mostafa A, et al. Acute behavioural disturbance associated with phenibut purchased via an Internet supplier. *Clin Toxicol (Phila).* 2015;53:636–638.

## 180. Peridural accidental administration of xenobiotics: an unpredictable outcome

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**Objective:** Peridural or intrathecal administration of xenobiotics may result in potentially severe adverse effects depending on factors that influence the toxicity (e.g. dosage, osmolarity, lipophilicity, baricity). Overdose or erroneous administration of a xenobiotic unintended for peridural administration may not follow predictable pharmacokinetic models.[1] We describe two cases of peridural erroneous injection for which, regards this specific route of

administration, data in medical literature are lacking. **Case report:** Case 1: A 72-year-old female, underwent a surgical hysterectomy, and erroneously received via peridural catheter 100 ml of sodium chloride solution 0.9% with ketorolac 30 mg, esomeprazole 40 mg and cefotaxime 500 mg infused over 9 hours. At the end of infusion she experienced severe burning lumbar pain, hypertension and mild lower limb edema. Clinical manifestations resolved during the next 2 days and no specific treatment was been applied. No sequelae were reported at one month follow up. Case 2: A 59-year-old male, underwent gastrectomy, and mistakenly received a parenteral nutrition mix (CLINIMIX N9<sup>®</sup>) (estimated amount 50 ml) in 30 minutes when the intravenous delivery was inadvertently connected to the peridural catheter. The patient manifested immediate abdominal pain and a liquor lavage with sodium chloride solution 0.9% at 5 mL/h for 48 hours was performed. No other clinical effects were reported and he was discharge after two weeks. **Conclusion:** Erroneous administration of a xenobiotic not registered or routinely used via the peridural (and intrathecal) route may require prompt and urgent intervention aimed at immediate withdrawal of cerebrospinal fluid. Cases with uncertain outcome and not previously described should be considered and managed as potentially fatal. With beta-lactam antibiotics neuro-excitatory features (convulsions due to their  $\gamma$ -aminobutyric acid antagonist properties) have been reported.[1] Our data, even if single experiences, describe a favorable clinical evolution of cases. Medical error is possible despite standardization of procedures, and confusion can arise with specialized and exclusive products available for peridural/intrathecal injection. Several factors influence the clinical toxicity of xenobiotics given peridurally, and a multidisciplinary approach is necessary in order to correctly evaluate and manage such cases.

## Reference

- [1] Rama BR. Intrathecal administration of xenobiotic. In: Hoffman RS, Howland MA, Lewin NA, et al, eds. Goldfrank's Toxicologic Emergencies. 10th ed. New York, USA: McGraw-Hill Education, 2015:703–10.

## 181. Adverse events related to the administration of two different formulation of long-acting injection antipsychotics

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**Objective:** Long-acting injections (LAI) of antipsychotic drugs are used in psychiatric practice for treating patients with non-adherence/partial adherence to oral pharmacotherapy. Most of these drugs are conjugated to fatty acids or other components that confer slow release properties when administered by intramuscular (depot) injection. However, direct entry into the bloodstream can occur during administration. We describe a case series of adverse events during administration of antipsychotic LAI in order to identify differences in severity and risks with olanzapine and haloperidol LAI. **Case series:** Olanzapine-LAI (OLA/LAI): We describe four cases of PIDS (post-injection delirium/sedation syndrome) after intramuscular administration of olanzapine-LAI.

These effects are probably due to entry of the drug into a blood vessel during injection. Case 1: Thirty minutes after injection of 300 mg a 49-year-old man was lethargic (Glasgow Coma Scale 8–9) with sinus tachycardia (150–160 beats/min) requiring beta-blockade. He improved 12 hours later and was completely recovered after 24 hours. Case 2: A 50-year-old woman in therapy with OLA/LAI for one year, developed paresthesia, confusion, disorientation and mood swings (aggressiveness and depression) after the 13th dose. She recovered with symptomatic treatment. Case 3: During the first OLA-LAI dose (405 mg) a 38-year-old man developed drowsiness that persisted for 12 hours. Case 4: Ninety minutes after OLA-LAI 300 mg rapid intramuscular administration, a 63-year-old woman had agitation, akathisia and QT prolongation (492 ms) which resolved with symptomatic treatment. Haloperidol-LAI: Case 1: A 55-year-old man erroneously received a 50 mg vial of haloperidol decanoate in a 1 hour infusion. Serum haloperidol was undetectable 8 hours later. Patient was asymptomatic and returned to the psychiatric ward the day after. Case 2: A 89-year-old woman received 50 mg haloperidol decanoate by intravenous instead of intramuscular injection. Serum concentration was 1.1 ng/mL one hour after administration and was undetectable 24 hours later. She was monitored for two days but had no neurological impairment or rhythm disturbances. Haloperidol serum concentrations were assayed using high performance liquid chromatography (limit of detection 0.5 ng/mL). **Conclusion:** PIDS is related to the rapid dissolution of the olanzapine pamoate salt in blood vessels, while haloperidol decanoate requires an esterase enzyme to act. Consistent with these findings, adverse events can occur even after correct administration of olanzapine LAI, but even if haloperidol decanoate is intravenously administered, neither clinical effects nor elevation in serum concentrations are expected.

## 182. Resurgence of propylhexedrine abuse as an inexpensive and legal alternative to methamphetamine use

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**Objective:** To describe a case of toxicity related to a classically abused medication, propylhexedrine, and an uncommon method of drug delivery. **Case report:** A 28-year-old male with a history of bipolar disorder, anxiety, and polysubstance abuse presented to an urban emergency department after ingesting one intact 250 mg propylhexedrine-soaked cotton rod. The patient reported smoking methamphetamine earlier in the day but then ran out. He purchased a propylhexedrine nasal inhaler and disassembled it to obtain the propylhexedrine-soaked cotton rod inside. He proceeded to ingest the entire cotton rod in an effort to achieve a methamphetamine-like high. He developed severe chest pain that prompted him to go to the hospital. Upon arrival, he was anxious, tremulous, and agitated. His pulse was 120 beats per minute, respiratory rate 16/min, blood pressure 150/101 mmHg, and temperature 36.9 °C. An electrocardiogram (EKG) showed sinus tachycardia without any ST changes or abnormal QRS or QT intervals. Complete blood count and basic metabolic panel was normal except for sodium of 132 mmol/L and glucose 107 mg/dL. Urine drug screen was negative. The patient improved with 4 mg lorazepam, which resulted in normalization of vital signs and improvement in symptoms. The patient later stated that he frequently ingests propylhexedrine-soaked cotton rods as a suitable and less expensive alternative when he cannot purchase methamphetamine. **Conclusion:** Propylhexedrine is an over-the-counter sympathomimetic similar to methamphetamine that is packaged as a

nasal decongestant and weight loss supplement that was abused from the 1960s to the 1980s for its stimulant effect. Propylhexedrine's only structural difference from methamphetamine is the substitution of an alicyclic cyclohexyl group in place of the aromatic phenyl group of methamphetamine. It is not, therefore, classified as a cycloamine and not a phenylephrine or amphetamine. It is legal to purchase in the US and easily purchased through Internet sites such as eBay and Amazon. This case is unique in that demonstrates a possible renewed interest in the abuse of a medication that has not been commonly reported in several decades. Additionally, our patient chose to ingest the entire propylhexedrine-soaked rod instead of a more commonly accepted method of extracting the medication and then ingesting or injecting the resulting liquid. Clinicians should be aware of the resurgence and methods of abuse, including ingestion of the entire medication delivery rod, of propylhexedrine as the prevalence of methamphetamine abuse continues to rise globally.

### 183. QRS prolongation and ventricular tachycardia after citalopram overdose in a pediatric patient

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**Objective:** Citalopram and its active metabolites are known to be potent QT-prolonging substances; however, their effect on the QRS interval in overdose is less clear. Case series have identified seizures and QT prolongation occurring in a dose-dependent manner, but only a minority of patients develop QRS widening, with no note of "serious arrhythmias or clinically significant hypotension".<sup>[1]</sup> We report a case of severe cardiac toxicity following a citalopram overdose corroborated by serum drug concentration. **Case report:** A 17-year-old female with a history of depression presented to the Emergency Department after a syncopal event at a party followed by generalized tonic-clonic movements. Her only endorsed exposure was recreational marijuana use. She was tachycardic (103–124 beats per minute) and hypotensive (96/50 mmHg). Her electrocardiogram (ECG) showed a maximum QRS duration of 132 ms (baseline QRS 86 ms) and QTc of 636 ms. She had multiple premature ventricular contractions, which progressed to 30 beats of ventricular tachycardia. She was treated with an amiodarone bolus, followed by multiple boluses of sodium bicarbonate and a continuous infusion. She had interval resolution of the abnormal QRS 7.5 hours from time of presentation, and her QT interval normalized by hour 79. Comprehensive urine drug screen by gas chromatography-mass spectrometry (GC-MS) was negative except for a citalopram concentration of 1100 ng/mL (normal steady-state serum concentration 9–200 ng/mL). **Conclusion:** Toxic effects of citalopram include seizures and ECG abnormalities, namely QT prolongation, but also include QRS widening with potential for malignant ventricular dysrhythmia.

#### Reference

- [1] Personne M, Sjöberg G, Persson H. Citalopram overdose—review of cases treated in Swedish hospitals. *J Toxicol Clin Toxicol.* 1997;35:237–240.

### 184. Adult clonidine overdose: prolonged bradycardia and central nervous system depression, but not severe toxicity

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**Objective:** Clonidine was originally used as an antihypertensive, but is now used in patients with substance abuse and in attention deficit hypersensitivity disorder. Most studies have been in children and there are limited reports of adult clonidine overdose. The study aimed to describe the clinical effects of clonidine overdose in adults. **Methods:** A review of a prospective cohort of poisoned patients who took a clonidine overdose (>200 mcg). Demographic information, clinical effects, treatment, complications (central nervous system effects, cardiovascular effects), and length of stay were extracted from a clinical database. **Results:** There were 133 admissions for clonidine overdose from January 1988 to September 2015. In 37 patients clonidine was ingested alone and in the remainder there were 1 to 8 coingestants. The commonest coingestants were benzodiazepines, alcohol, antipsychotics, opiates and antidepressants. Of 133 patients 78 (59%) were female, and the median age of participants was 27 years (range 14–65 years). The median dose taken was 2000 mcg (400–15,000 mcg). There was a decreased level of consciousness (Glasgow Coma Scale [GCS] < 15) in 75 of 133 (56%) admissions, and coma (GCS < 9) in 12 (9%). Miosis occurred in 34 (26%) patients. Bradycardia (heart rate < 60 bpm) occurred in 78 (59%) patients and persisted for a median of 20 hours (3 to 58 hours;  $n=57$ ). Two patients had early severe hypertension (systolic blood pressure [BP] > 180 mmHg). Hypotension (BP < 90 mmHg) occurred in 23 of 133 (17%). Hypothermia (temperature < 35 °C) was present in 10 patients. There were no deaths. The median length of stay was 21 hours (interquartile range 14–35 hours). Thirty one patients were admitted to the intensive care unit. Thirteen of these were intubated and ventilated, but none ingested clonidine alone. Treatments included activated charcoal in 14, atropine in 11 and naloxone in 13. None of the 13 patients given naloxone responded (no change in GCS and no change in heart rate). The use of naloxone was associated with a longer length of stay. **Conclusion:** Clonidine commonly causes central nervous system depression and bradycardia, while severe effects such as hypotension and coma were uncommon. Clonidine alone appears to rarely cause significant respiratory depression; none required ventilatory support. Naloxone was not associated with improved outcome.

### 185. Elevation of blood urea nitrogen with initiation of arginine chloride supplementation

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**Objective:** Metabolic alkalosis is a common entity in the pediatric cardiac intensive care unit. In many instances contraction alkalosis can be treated with chloride supplementation. We present a case of contraction alkalosis treated with arginine chloride that developed a markedly elevated blood urea nitrogen (BUN) prompting pediatric nephrology consultation for acute kidney injury. **Case report:** A 5-month-old, 3.8 kg female, with a history of trisomy 21 and ventricular septal defect (VSD) repair, was hospitalized for mediastinitis. She was intubated for respiratory distress and treated with intravenous (IV) fluids, along with IV vancomycin, cefepime and an epinephrine infusion. Pulmonary hypertension and pulmonary edema prompted treatment with furosemide and chlorothiazide IV infusion, in addition to inhaled nitric oxide (iNO), milrinone and sildenafil. Due to developing hypochloremic metabolic alkalosis she was started on acetazolamide along with potassium chloride and sodium chloride supplementation in her enteral feeds. Hypochloremia and metabolic alkalosis persisted and the furosemide and chlorothiazide infusions were tapered and arginine chloride 20 mmol was given IV every 6 hours. Four hours after the initial dose, the BUN rose from 26 mg/dL to 44 mg/dL (reference 7–19 mg/dL). She received 3 subsequent doses of arginine chloride over the next 18 hours; the BUN increased further to 82 mg/dL and the arginine chloride was discontinued. Aspartate aminotransferase (AST) was 55 U/L (reference <35 U/L), alanine aminotransferase (ALT) was 36 U/L (reference <55 U/L) and ammonia 49 µmol/L (reference 21–50 µmol/L). The BUN peaked at 121 mg/dL 9 hours later and returned to baseline 2 days later with supportive care. Creatinine rose from 0.5 mg/dL to 0.8 mg/dL (reference 0.6–1.1 mg/dL) during this time period but also returned to baseline within 2 days. **Conclusion:** Persistent metabolic alkalosis while on loop and thiazide diuretics prompted chloride supplementation for contraction alkalosis. Despite potassium chloride and sodium chloride supplementation in enteral feeds, metabolic alkalosis persisted, prompting supplementation with arginine chloride which is listed in standard pediatric clinical references as a potential treatment for metabolic alkalosis. Arginine is an amino acid and is metabolized to ornithine and urea. Increases in BUN may occur primarily in patients with renal impairment due to decreased elimination of urea. With no prior reported cases, clinicians should be aware that arginine supplementation for the treatment of contraction metabolic alkalosis may result in uremia with a normal creatinine, and consider this side effect prior to implementation.

## 186. Ocular cyclopentolate: another cause of toxic acute confusional state

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**Objective:** Cyclopentolate hydrochloride is a mydriatic, cycloplegic, muscarinic antagonist. It is used during eye examinations. Since 1902, only 76 cases of neurotoxicity related to the administration of anticholinergic eye drops have been reported, 30 involved cyclopentolate. It is estimated that only 1–5% of the active ingredient of the eye drops penetrates the eye, although 80% may pass to the general circulation through the nasolacrimal, conjunctival and uveoscleral routes, either directly or indirectly after absorption by the digestive tract.[1] From the general circulation, cyclopentolate may cross the blood-brain barrier to the central nervous system. Systemic anticholinergic clinical manifestations (dry skin and mucous membranes, facial flushing, acute

urinary retention, fever) are rare: cardiovascular (tachycardia and hypertensive crisis) and neurotoxic (acute delirium, psychomotor agitation, ataxia, abnormal language, hallucinations, convulsions, and coma) effects are more prevalent and normally abate when the active substance is eliminated (approximately 12 hours after instillation). We report a patient with acute confusion after administration of cyclopentolate eye drops. **Case report:** A 75-year-old woman was transferred from an eye clinic to our emergency department due to sudden disorientation and psychomotor agitation. The patient had attended the clinic for a retinal arteriography 90 minutes earlier. Pupillary dilation was provoked by instillation of a couple of drops of cyclopentolate 1% in each eye. On admission, the patient was conscious, disoriented in time and space, and had intense agitation, incoherent speech and dysarthria. The patient had mydriatic and reactive pupils and a murmur in the aortic area. Blood pressure was 143/56 mmHg, heart rate 92 pm, temperature 37.7 °C, oxygen saturation 94%, and blood glucose 163 mg/dL. Electrocardiogram (ECG) showed sinus rhythm with Q wave in lead III. A computerised tomography (CT) scan showed no significant alterations and all analytical tests were within normal parameters except for troponin I (0.13 ng/mL). The patient required sedation with intravenous midazolam for symptom control and was admitted to the intensive care unit for observation. After an acute episode lasting 10 hours, she was neurologically and cardiovascularly stable. At 24 hours, troponin peaked at 2.7 ng/mL without ECG changes or cardiac signs. **Conclusion:** Topical anticholinergics may provoke neurotoxic and cardiotoxic manifestations. In addition, no previously reported case has described impaired markers of myocardial damage in patients without underlying heart disease.

## Reference

- [1] Jiménez-Jiménez FJ, Alonso-Navarro H, Fernández-Díaz A, et al. [Neurotoxic effects induced by the topical administration of cycloplegics. A case report and review of the literature.] [Article in Spanish] *Rev Neurol.* 2006;43:603–609.

## 187. Adverse drug reactions reported to the Poison Control Centre of Morocco (2013–2014)

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**Objective:** Poison information centres may be contacted by physicians and the public for advice on both drug overdoses and adverse drugs reactions (ADR). In Morocco, this role of managing ADRs by the poison control centre is facilitated by the existence of the pharmacovigilance and toxicovigilance centres in the same premises. The aim of this study was to describe the epidemiological features of human ADRs reported to the Moroccan Poison Control and Pharmacovigilance Centre (CAPM) between 2013 and 2014. **Methods:** We conducted a retrospective study including all cases of ADR reported by telephone to the CAPM from 1 January 2013 to 31 December 2014. The data included age distribution, sex, symptomatology and the outcome. **Results:** The CAPM received enquiries on 352 ADRs (5.8% of medication poisoning cases). The public reported 128 of these. Of the notifications from

healthcare professionals, 90% came from emergency departments. The average age of patients was  $30.4 \pm 21.4$  years and the sex ratio (M/F) was 1.03. Two classes of drugs were incriminated in 14.2% of adverse reactions. The drugs implicated in the largest number of ADRs were antidepressants (13.3% of cases) followed by antimicrobials (12.7% of cases). The main adverse reactions reported were skin manifestations (19.5% of cases) and digestive signs (15.2% of cases). Overall 8.2% of cases required hospitalization. One death was reported and the drug involved was midazolam. **Conclusion:** Poison control centres play an important role in the reporting of the adverse drug reactions and in their management.

## 188. Botulism cases in Austria, 2006–2014

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**Objective:** Botulism caused by toxins produced by *Clostridium botulinum* is a rare but life-threatening disease. We evaluated human botulism cases in Austria from 2006 to 2014. **Methods:** Discharge diagnoses from Austrian hospitals, cases of human botulism registered by the Austrian Agency for Health and Food Safety, and cases reported to the Poison Information Centre were evaluated from 2006 to 2014. **Results:** In 32 cases (29 adults and three children aged 3 months, 8 months and 2 years) botulism was suspected based on their symptoms. In adult patients the most common primary symptoms reported were diplopia, ptosis, difficulty in accommodation, xerostomia, dysphagia and dysarthria. In 9 cases mouse bioassays were positive for botulinum toxin. In 4 cases serotypes were classified and serotype B was isolated in 3 cases. In one case the causative source suspected was home-made smoked meat. In one patient who required mechanical ventilation for 9 days, serotype E was confirmed. In this case the consumption of a smoked, vacuum-packed trout was assumed to be the source. The 3-month-old infant was restless, refused to drink and suffered from loss of head control, xerostomia and dysphagia. A stool sample in this patient was positive for subtype B toxin. The causative agent could not be found. This child recovered after receiving antitoxin and symptomatic treatment. This was the first case of infant botulism verified in Austria (2013). The 8-month-old infant developed muscle weakness, loss of head control, mydriasis and respiratory paralysis. Botulinum toxin type B was isolated from a stool specimen. The infant recovered without sequelae after receiving antitoxin and mechanical ventilation for several weeks. The source could not be identified. The 2-year-old child showed several unspecific symptoms. All samples were negative and he recovered after symptomatic treatment. **Conclusion:** The diagnosis of human botulism can be challenging due to partially unspecific and diverse symptoms and the variable severity of the disease. In most cases a differential diagnosis excluding other neurologic diseases is necessary. As the laboratory confirmation via mouse bioassay takes about five days in Austria, the most important therapy is intensive care treatment. Antitoxin is given very rarely.

## 189. Human exposures to opioid analgesics reported to the Poisons Information Centre Erfurt from 2005 to 2014

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**Objective:** In Germany, the number of prescriptions of opioid analgesics (OA) dispensed increased from the beginning of 2004 to the end of 2013 by 45% and fell slightly in 2014.[1] Therefore, we asked whether a similar development could be observed in cases of OA exposures registered by the Poisons Information Centre (PIC) Erfurt. **Methods:** The changes in frequencies, circumstances of exposure, symptoms, symptom severity, age groups, and substances involved in all OA-related enquiries to the PIC Erfurt were analysed retrospectively from the beginning of 2005 to the end of 2014 and compared to non-OA (NOA) exposures. **Results:** In total, 1909 and 9526 cases of OA and NOA exposures were registered. In 925 and 5225 cases, only one OA or NOA was involved. Although OA and NOA exposures increased by almost 50% and 32.8% from 166 and 832 in 2005 to 247 and 1105 in 2014, the percentage of all cases of exposure remained almost constant at 1.3% (1.1–1.5%) and 6.7% (6.5–7.1%), respectively. The most frequent OA were tramadol ( $n=718$ ) and tilidine ( $n=395$ ). While tramadol exposures showed no certain trend (median: 73.5; range: 57 to 86), tilidine exposures doubled from 29 in 2005 to 60 in 2014. OA exposures occurred commonly in adults (90.4%) and less frequently in children (9.5%; toddlers 4.1%) compared to NOA exposures (adults 67.6%; children 32.3% [toddlers 15.2%]). The proportion of intentional abuse exposures was higher in OA (5.7%) than in NOA exposures (0.4%), whereas the proportion of accidental and suicidal exposures was lower (14.6% and 52.6% versus 20.9% and 58.5%). OA exposures were more often symptomatic (mild 48.4% versus 27.3%; moderate 13.4% versus 4.3%, severe 6.8% versus 1.2%) than NOA cases. Of 27 cases with seizures, 24 involved tramadol. **Conclusion:** OA exposures correlated only partially with the number of prescriptions dispensed. Tramadol and tilidine were involved most often. While the absolute numbers of tramadol exposures remained almost constant, the cases with tilidine increased twofold. Compared to NOA exposures, OA exposures resulted more often in moderate and severe symptoms. The high potential of tramadol to cause seizures has already been described in the literature.[2]

## References

- [1] Böger RH, Schmidt G. Analgetika. In: Schwabe U, Paffrath D, eds. Arzneiverordnungsreport 2014. Springer-Verlag Berlin-Heidelberg, Germany; 2014:301–319.
- [2] Ryan NM, Isbister GK. Tramadol overdose causes seizures and respiratory depression but serotonin toxicity appears unlikely. Clin Toxicol (Phila). 2015;53:545–550.

## 190. Palytoxin exposures reported to the US National Poison Data System (NPDS)

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**Objective:** Palytoxin is one of the most potent toxins known. It is produced by the microalgae *Ostreopsis* and can result in death after consumption of fish containing the poison. While ingestion can result in systemic toxicity and death, much less is known about clinical symptoms when exposed through dermal and inhalational routes, typically from exposure to coral. The purpose of this study was to describe and compare the symptoms of dermal and inhalational palytoxin exposures reported to the US National Poison Data System (NPDS). **Methods:** The NPDS was queried for all dermal and inhalational palytoxin exposures reported to US poison centers between 2003 and 2014. Data analyzed included demographic and exposure characteristics. Differences in select clinical effects and therapies were evaluated for single route of exposures through chi-squared analyses. **Results:** Of the 171 exposures reported, 116 (67.8%) were dermal only, 44 (25.7%) were inhalational, and 11 (6.4%) were both. The majority of exposures occurred in adults 20–39 years of age ( $n = 79$ , 46.2%), males ( $n = 137$ ; 80.1%), occurred at a residence ( $n = 147$ ; 86.0%), and were accidental [e.g. accidents, occupational, bites/stings ( $n = 152$ ; 88.9%)]. Approximately one-third of cases were managed outside a healthcare facility, while most cases managed at a healthcare facility were treated, evaluated and released ( $n = 57$ ; 33.3%). Cases that were exposed dermally were more likely to have edema (11.2% versus 0.0%;  $p = 0.021$ ) or irritation/pain (25.9% versus 0%;  $p < 0.001$ ). Inhalational exposures were more likely to have coughing/choking (34.1% versus 0.9%;  $p < 0.001$ ), dyspnea (54.5% versus 4.3%;  $p < 0.001$ ), fever/hyperthermia (61.4% versus 6.9%;  $p < 0.001$ ), muscle weakness (18.2% versus 2.6%;  $p < 0.001$ ), tachycardia (20.5% versus 6.9%;  $p = 0.013$ ) and vomiting (18.2% versus 6.0%;  $p = 0.019$ ). **Conclusion:** Though palytoxin exposure is rare in the US, dermal exposures were more frequently reported to NPDS and were associated with mostly benign clinical effects. Inhalational exposure was associated with more notable toxicity, although most symptoms were also relatively benign. Supportive care and bronchodilator therapy is the mainstay of treatment for inhalational exposure, while dermal irritation is managed with irrigation and washing. Given that most occurrences were documented as unintentional exposure at a residence, there needs to be better education about the dangers of palytoxin-containing coral as well as preventative measures for aquarium technicians and enthusiasts to prevent further exposures. As NPDS is a passive surveillance system, exposures may be under-reported and the data presented here may underestimate the true burden.

## 191. How can Poison Control Centers detect new trends in health? Vitamin D exposures as an example

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**Objective:** The prescription of vitamin D supplements has risen in recent years owing to increased awareness of vitamin D

deficiency. We hypothesize a change in the epidemiology of overdoses that could be detected by the Poison Control Center (PCC). **Methods:** This was a retrospective analysis of data from our PCC to evaluate trends of exposures to vitamin D over the period 1 January 2005 to 30 June 2015. Cases were limited to human exposures involving vitamin D as a single substance. **Results:** Over the study period 1869 consults related to vitamin D (vitamin D3 2000 UI/ml or 5-hydroxyvitamin D 0.266 mg or 3 mg/ampoule) met the inclusion criteria. An increase of cases per month was observed from 9.6 in 2005 to 35.8 in 2015 (a 3.7 times increase). The majority of patients were male (58.7%) and infants (66.1%). Mean age was 6.1 years. In 2005, 66.3% of cases were related to infants (<1 year old) and 3.4% were adults. In 2015 the data were 45.9% and 36%, respectively, an increase in the percentage of adults of more than 10 times. The reasons for exposure were double or triple dosing 47.3%, intoxication 19.5%, wrong dose 14.4%, wrong route 2.5%, medication administered to the wrong patient 0.4% and other 15.9%. In adults the predominant reason was intoxication (29.3%) followed by double-triple dosing (28.6%). In infants and toddlers (<2 years) the percentages were 18.9 and 69.3%, respectively. Only 8 cases were estimated as major outcome, with 34 moderate outcomes. Infants had proportionally less risk of having severe medical outcomes; 18 moderate or major outcomes (1.8% of infants), whereas the percentage within this age group was 4.3% for children between 1–14 years, and 5.1% for adults. Clinical effects at the time of the consult were primarily gastrointestinal with vomiting ( $n = 12$ ), nausea ( $n = 6$ ), diarrhea ( $n = 6$ ), abdominal pain ( $n = 3$ ) and constipation ( $n = 1$ ), asthenia and headache (8 cases each), hypertension and dizziness (3 each), hypercalcemia ( $n = 2$ ), and others (myalgia, dry mouth, ataxia, tachycardia, agitation, delirium, anorexia [1 each]); however most patients were asymptomatic (96.5%). Most enquiries were received from the public (87.3%); of these 94.2% were managed at home. **Conclusion:** Our data demonstrate an emergence of vitamin D overdoses in adults. Although the toxic exposure to this vitamin carries a very small risk, awareness regarding a cautious use of supplements can prevent it.

## 192. Exposures to drugs used to treat attention deficit hyperactivity disorder (ADHD): a Poison Control Center experience

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**Objective:** Prevalence of attention deficit hyperactivity disorder (ADHD) among children and adolescents is approximately 5–12% in Spain. Currently, atomoxetine, lisdexamphetamine, modafinil, and methylphenidate are used to treat this psychiatric disorder but these can also be diverted for recreational purposes. There are few statistical data on exposures to these drugs in our community. Therefore our aim was to investigate the circumstances of toxic exposures to ADHD therapeutic drugs. **Methods:** From April 2005 to September 2015, the Spanish Poison Control Center registered human toxic exposures to atomoxetine, lisdexamphetamine, modafinil, and methylphenidate. Consults on veterinary cases (28) and those related to pharmacological questions (282) were excluded. Data was collected retrospectively on a standardized form including age and gender of each patient, causes of poisoning, route of exposure and clinical manifestations. **Results:** During the study period 2165 cases met the inclusion criteria. The most frequent drugs were methylphenidate (90.1%), atomoxetine (7.7%), lisdexamphetamine (1.4%), and modafinil (0.7%). Exposure

to more than one substance (poly-substance) was reported in 7.6% of consults. Most patients were male (57.6% male, female 24.5%, and 17.9% unknown). The age range of patients was 6 months-75 years; of these 58.2% were children >2-14 years, 26.3% were >14 years, 5.7% were ≤2 years and 9.8% unknown. Mode ages were 8 and 10 years (5.8% each). Calls were received most frequently from the general public (60% of cases), followed by hospitals (25.3%), primary healthcare units (12.6%), other (1.3%) and unknown (0.6%). Oral was the main route of exposure (76%). The majority of exposures (66%) were accidental (non-intentional) and 11.2% were intentional. The circumstances of cases involving intentional exposure were suicidal (66.5% of this group), abuse (11.9%, of which 64.2% were male, range age 15-45 years) and other (21.5%). At the time of the consult clinical manifestations were present in 11% of cases, 70.2% of them had neurological signs and symptoms, 27.3% had cardiovascular signs, 6.3% gastrointestinal, 3.4% dermal, 2.1% ocular and 2.9% other. The outcome estimation was asymptomatic 9.3% of consults, mild 33.4%, moderate 18.2% and severe 1.7%. **Conclusion:** Our poison control center has received a significant percentage of moderate to severe exposures to drugs for ADHD. Although a limitation to this study included its voluntary and retrospective nature, data should alert paediatricians and psychiatrists to assess for the risks of ADHD drugs, which have a relatively narrow therapeutic index.

### 193. Risks of silica gel in medicine containers: the example of a vitamin D and *Lactobacillus* product for new borns

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**Objective:** Over a two month period in 2015 the Danish Poisons Information Center (DPIC) saw a sudden increase in the number of enquiries from parents who had given their new born babies a vitamin D/*Lactobacillus* combination product. They were concerned as they had inadvertently made up the mixture ready for use by adding the silica gel that was placed in a small bag in the package into the vitamin D oil solution instead of the *Lactobacillus* that was separately placed in the bottle cap. The product description indicated that the oil solution would be cloudy after adding *Lactobacillus*, which was only partly soluble. According to the Danish Health Authority the daily recommended vitamin D dose in babies (>2-weeks-old) is 10 micrograms, equivalent to 5 drops.[1] There are no specific recommendations on *Lactobacillus* dosing for infants, but studies have shown that *Lactobacillus* may have a beneficial effect on atopic dermatitis [2] and colic.[3] **Methods:** Enquiries to the DPIC regarding the vitamin D drops/*Lactobacillus* product up to 31 October 2015 were analysed. **Results:** There were 19 enquiries from parents who prepared the mixture incorrectly. The first enquiries were received at the beginning of September 2015. Often the parents were not aware of the mistake for some time (days). In two cases the product was used for 3 and 6 weeks, respectively, before the error was realised. Fortunately none of babies were unwell after being fed the incorrectly made mixture, but they did not receive the *Lactobacillus*. **Conclusion:** As a result of the many enquiries received the manufacturer issued an alert to all pharmacies encouraging them to provide information to parents on how to make up the product correctly.[1] The vitamin D/*Lactobacillus*

product was first marketed in 2014, but the first batch containing silica gel in the package was not available until mid-2015. From 2016 there will be a warning sign on the silica gel bag stating that it should be discarded. Moreover, a pre-mixed vitamin D/*Lactobacillus* product is being prepared.[4]

### References

- [1] Prevention, diagnosis and treatment of Vitamin D deficiency; [cited 2015 Nov 4]. [Website in Danish] [https://sundhedsstyrelsen.dk/da/sundhed/ernaering/~/\\_media/FA2FC43A29D146918C9695BE\\_C2716A33.ashx](https://sundhedsstyrelsen.dk/da/sundhed/ernaering/~/_media/FA2FC43A29D146918C9695BE_C2716A33.ashx)
- [2] Rosenfeldt V, Benfeldt E, Nielsen SD, et al. Effect of probiotic lactobacillus strains in children with atopic dermatitis. *J Allergy Clin Immunol.* 2003;111:389-395.
- [3] Savino F, Bailo E, Oggero R, et al. Bacterial counts of intestinal *Lactobacillus* species in infants with colic. *Pediatr Allergy Immunol.* 2005;16:72-75.
- [4] Personal communication, 2 November 2015. Chief Executive Officer, Søren Thomsen Biocare Copenhagen.

### 194. An epidemiological study of acute intoxications treated in a second level, recently-opened hospital between 2010 and 2015

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**Objective:** Acute intoxication (AI) is one of the most common clinical situations in emergency departments. An increase in the number of toxicological events has been observed in recent years. Our study describes the epidemiological and toxicological characteristics of AI in patients admitted to a hospital emergency room. **Methods:** A descriptive and retrospective analysis of intoxications diagnosed between 2010 and 2015 in a second-level hospital with a population zone of 350,000 inhabitants. Medical records were reviewed to collect demographic characteristics, intoxication type, treatment and outcome. The statistical analysis was carried out using SPSS. **Results:** In total 2058 patients were included, with an average age of  $36 \pm 5$  years (56% women). This figure represents 1.1% of the total emergency admissions in this period. The incidence was maximal in November, December and January. The most frequent toxicological agents were drugs 943 (46%), most commonly psychiatric medication (811, 48%). Overall the most common drugs were benzodiazepines ( $n=500$ , 53%), antidepressants ( $n=141$ , 15%) and antipsychotics ( $n=94$ , 10%). The second most common substances were ethanol ( $n=665$ , 22%) and drugs of abuse ( $n=205$ , 10%), of which cocaine ( $n=98$ , 48%), cannabis ( $n=51$ , 25%) and heroin ( $n=23$ , 11%) were most common. Intentional exposure occurred in 71% ( $n=1456$ ) of cases. A third of patients ( $n=669$ , 33%) received gut decontamination (most frequently activated charcoal 67% and gastric lavage 33%) while a quarter ( $n=504$ , 24%) received antidote treatment. Urine screening was carried out in 21% ( $n=426$ ) of patients. Admission to intensive care was required in 32 cases (6.5%). A judicial report was carried out in 478 (23%) of cases. The mortality rate was 0.2% ( $n=5$ ). **Conclusion:** The number of detected intoxications increased during the observational period. While medical drugs remain the main agents, drugs of abuse have decreased. The use of gastric lavage and urine screening has decreased as a

result of improvement actions. The mortality rate from AI was low in our population. This study establishes the importance of the profile in acute intoxications in our environment, which is necessary to improve the quality of our department and more efficient prevention.

## 195. Severe accidental intoxication: a 10-year analysis

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**Objective:** Accidental intoxications with severe clinical course are rare.[1] Knowledge of risk factors and agents is essential for treatment and prevention. This study presents analysis of 10 years' of data from a single poison center to identify the risk factors for severe poisoning. **Methods:** An explorative data analysis of human intoxications reported to the Poison Center in Mainz from 2005 until 2014. Inclusion criteria were defined as accidental intoxications with a Poisoning Severity Score (PSS) of 3 (severe), a validated exposure, possible causality and successful follow up. **Results:** Of 265,423 reported human cases during the 10 year period 168,302 were accidental, 502 of those reached an PSS of 3, 208 of those had a successful follow up and finally 168 cases (0.06% of all) remained for further investigation after selecting data for validated exposure and possible causality. These included 168 cases covered 140 survivors and 28 cases with a fatal outcome. Differentiation to age groups showed a peak in infants (median age 2 years) and a slight increase in patients over 65 years. These age groups show a disposition for certain agents. In infants ( $n=34$ ) severe accidental intoxications was commonly associated with pharmaceutical products (32.4%), corrosive cleaning agents (29.4%) and lamp oil (26.5%). Incidents in adults ( $n=65$ ) often involved inflammable gas inhalation (20%) and self-collected and misidentified food (especially herbs and mushrooms) (20%). Risks for the elderly (age over 65 years) ( $n=54$ ) were self-administration of an incorrect medicine or overdosage of pharmaceutical products (38.9%). This age-group also presented with a high number of intoxications with cosmetics, soaps and disinfectants/germicides (14.8%). **Conclusion:** Accidental intoxications per se are numerous, but only a small number result in severe clinical progression (PSS 3). For improved identification of the substances involved, the circumstances of exposure and identification of persons at risk (toxicovigilance) a national monitoring of severe accidental intoxications is required as a basis for a prevention strategy. This could be provided by national Poison Centers if adequate personnel resources are available.

### Reference

- [1] AAPCC. 2013 Annual Report of the NPDS [cited 2015 Nov 4]. Available at: <http://www.aapcc.org/annual-reports/>

## 196. Acute poisoning in addicted patients in the toxicology department

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**Objective:** To analyse the characteristics of acute poisoning cases of both alcohol and other psychoactive drugs in addicted patients, admitted to the Toxicology Department, Emergency University Hospital "Pirogov", between January 2012 and December 2014. **Methods:** A 3-year retrospective study was conducted. Patients over 18 years of age with acute alcohol and poisoning with psychoactive drugs were studied. Data were retrieved from hospital records. We analysed the etiological and demographic characteristics of the acutely poisoned patients. The substances include alcohol and illicit drugs such as opiates, cannabinoids, cocaine, amphetamines and hallucinogens. The presence of alcohol and psychoactive substances was determined by thin-layer chromatography. All patients with intoxication by illicit drugs had physical and psychological dependence. The evaluation was carried out according to the criteria for dependence of DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition). Of the patients with alcohol poisoning 72% were addicted, as assessed by the Clinical Institute Alcohol Withdrawal Assessment Scoring Guidelines (CIWA-Ar). **Results:** A total of 1327 patients over 18 years of age, admitted to the Toxicology Department were included; there were 339 (25.5%) females and 988 (74.5%) males. The frequency distribution of acute intoxications was alcohol 1088 (82.0%; females 21.6%, males 60.4%) and psychoactive substance 178 (13.4%, females 3.7%, males 10.5%). The combination of alcohol and illicit drugs was observed in 51 (3.8%) patients (females 0.3%, males 3.5%). The highest incidence of alcohol poisoning was found in 2013, involving more males than females. The largest number of patients was in the age group over 35 years, followed by those aged 26–35 years. The highest incidence of monotoxic poisoning with psychoactive substances was found in 2013, again involving more males than females. In comparison with alcohol abusers, drug abusers were younger. The largest number of patients was in the group aged 26–35 years, followed by those aged 19–25 years. The patients with mixed poisoning were evenly distributed in all age groups. A decrease in heroin poisoning was shown, however an increase in marijuana, amphetamines and methadone poisoning was observed during the 3-year study period. A fatal outcome was recorded in 14 cases (1.1%) with acute poisoning. **Conclusion:** Alcohol, cannabinoids, opioids and amphetamines are the most important drugs of abuse causing acute poisonings and requiring medical intervention.

## 197. Evaluation of biocidal product enquiries to the Austrian Poison Information Centre 2014

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**Objective:** A biocidal product is any substance or mixture intending to destroy, deter, render harmless, prevent the action of, or exert a controlling effect on any harmful organism by any means other than mere physical or mechanical action. Biocidal products are divided into four main groups: disinfectants, preservatives, pest control and other biocidal products. The European Union has set up strict rules and procedures to ensure a high level of protection for human health, animal health and the environment. **Methods:** On behalf of and funded by the Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management the local Poison Information Centre (PIC) retrospectively evaluated enquiries regarding exposures to biocidal products

in 2014. **Results:** PIC Austria received a total 25,000 telephone enquiries in the year 2014, including 529 regarding biocidal product exposure. Of these, 312 (59%) patients were under the age of 15 years, and 217 (41%) over 15 years of age. Accidental exposure occurred in most cases ( $n=502$ ); 15 cases were suicidal attempts and in 12 cases the exposures were due to other causes e.g. misuse. In most cases the product was taken orally ( $n=313$ ), in other cases it was inhaled ( $n=133$ ), in the patients' eyes ( $n=31$ ) or on the skin ( $n=29$ ). In 23 cases there was a combined exposure. In 433 cases a poisoning could be excluded due to minor exposure. Due to lack of information, in 68 cases the risk of intoxication could not be estimated at the time of consultation. In 14 cases intoxication was suspected and medical observation was recommended. In only 14 patients was intoxication verified due to the severity of the symptoms: 5 patients inhaled chlorine gas, 3 ingested hand disinfectant, one patient ingested a chlorinated sanitizer, one ingested copper sulfate, one had an ocular exposure to industrial disinfectant, one had chemical burns of the skin caused by an industrial disinfectant and two patients had chemical burns after dermal exposure with a sanitizing product for swimming pools. In nine cases the exposure took place at home; four were exposed at the work place and in one case in a hospital. **Conclusion:** In relation to the total number of calls, enquiries regarding biocidal products are relatively rare and the number of human intoxications seems to be small. Only 14 cases with severe symptoms which required medical treatment were recorded. No deaths were recorded in the cases reported to the local PIC.

## 198. Poison exposures in early teens: calls to the Finnish Poison Information Centre in 2014

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**Objective:** To study the poison exposures of adolescents aged 10–15 years based on calls to the Finnish Poison Information Centre (FPIC). **Methods:** A review of data from the Call Database of the FPIC and the National Population Register data for the year 2014. **Results:** The FPIC received 27,909 calls related to human poison exposures in 2014. Of these, 954 (3.4%) concerned poison exposures in adolescents aged 10–15 years (early teens), who comprise 6.5% of the total Finnish population. The incidence was therefore 270 calls/100,000 inhabitants in this age group. Older adolescents  $\geq 16$  years and adults comprise 83.6% of the total population and the FPIC received 9243 calls (33.1% of all calls) about this group, an incidence of 202 calls /100,000 inhabitants. While only 2% of the exposed early teens made the telephone call to the FPIC themselves, 43% of adults did. Concerning both age groups, up to one third of the callers came from healthcare professionals. At the time of the call, 40% of the exposed early teens had symptoms; one third (32%) received advice to visit a doctor immediately or were already under treatment, and one fifth (21%) were advised to visit a doctor if the symptoms persisted or worsened. The most common route of exposure was oral intake, but also eye, skin and airway exposures were documented. Of all exposures, 31% were intentional. The most common intoxicants were medicines, which comprised 55% of all exposures in the early teens. Also alcohols, petroleum products and solvents, plus acids and bases were listed in the top ten of agents. Of the exposure to medicines 50% were intentional. The majority of drugs were central nervous system (CNS) agents namely antiemetics, antipsychotics, hypnotics, anxiolytics or

antiepileptics. Although only 3.4% of exposures occurred in early teens, the age-group-related proportion of calls due to medicine exposure was 11%. Exposure to fluoxetine, cyclizine, risperidone and oxcarbazepine were particularly high, being respectively, 36%, 30%, 22%, and 19% of exposures to medicines in all age groups. **Conclusion:** FPIC calls due to suspected toxic exposure in 10–15-year-olds might be more frequent than those occurring in older teenagers or adulthood. One third of all exposures and a half of exposures to medicines were intentional. Only 2% of early teens made the call to the FPIC themselves, compared to 43% in adulthood. Drug exposure to CNS agents such as antipsychotics, anxiolytics and antiemetics seemed to be common.

## 199. Descriptive study of medical toxicology consultations at a teaching university hospital in Bangkok

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**Objective:** A medical toxicologist became available at our teaching hospital in 2012 then joined the Toxicology Investigator's Consortium (ToxIC) in August 2013. ToxIC is the American College of Medical Toxicology's research network mainly involved in the US healthcare setting. Our hospital is one of few outside the US in the network. Data collection in the ToxIC Registry can be useful in several ways such as research and resource management. Objectives were to describe toxicological cases seen at the bedside in a hospital in Bangkok and include their presentations and treatments provided. **Methods:** Data on epidemiology, toxic substance type, venomous organism species, clinical presentation, laboratory results, and treatment provided were collected prospectively at the bedside and were entered into the database. The study period was 1 August 2013 to 31 March 2015. **Results:** Annually, the hospital received approximately 80,000 Emergency Department visits. During the 20-month-study, 559 cases were registered in the toxicology logbook. This made our incidence of toxicological cases approximately 0.42%. Thirty-five of these cases were not recorded on ToxIC data sheets and not entered into the ToxIC registry. Data from 524 cases were included for further analysis. Of the 524 patients, 58% were male. The majority (59%) were between 19–65 years old, followed by 25% of cases who were aged 13–18 years. The primary reasons for the encounter were intentional pharmacological (41%), toxic animal (27%), and intentional non-pharmacological (12%) exposures. The major primary substance encounters were opioids (84 cases; 94% were tramadol). Of 143 toxic animal exposures, 52% and 21% involved snakes and centipedes, respectively. Regarding treatment, 11 cases underwent gastric lavage, 13 received single-dose activated charcoal, 10 received multiple-dose activated charcoal, and 1 underwent hemodialysis. The most common antidotes given were acetylcysteine (20 cases), thiamine (13 cases), naloxone (10 cases) and snake-antivenom (9 cases). **Conclusion:** Intentional exposure was the most common reason for toxicology encounters. The major substance was tramadol which is widely available over-the-counter in Thailand. On the other hand, envenomation was also a major cause of toxicological visits at this hospital, even though Bangkok is the most urbanized city in the country and this could give us a unique opportunity for envenomation research in an urban setting. Gastric lavage was still done, but in a small number of patients. This information is crucial for resource management and plans for establishing a formal and sustainable medical toxicology service at this teaching hospital.

## 200. Increased paracetamol-related calls to the Finnish Poisons Information Centre better reflect paracetamol sales than serious poisonings

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**Objective:** Recent studies have indicated that the number of paracetamol poisonings has been increasing in some countries.[1] We studied the changes in paracetamol-related queries to the Finnish Poison Information Centre (FPIC), and serious intoxications, involving hepatotoxicity or death in 2001–2014. These data were compared with paracetamol sales in Finland. **Methods:** A retrospective analysis of the FPIC database on calls, the national cause of death registry, the registries of liver transplantations and Molecular Absorbent Recycling System (MARS)-treated patients from the liver intensive care unit of the Helsinki University Hospital. Data on paracetamol prescription and over-the-counter (OTC) sales as defined daily doses (DDD) was obtained from the Finnish Medicines Agency. **Results:** Between 2001 and 2014 the number of calls/year to the FPIC related to human paracetamol exposures increased 5-fold from 227 to 1058. There was no significant change in the age distribution of the enquiries. Most of the calls involved minors: mean 58% (range 52–64%) for children under 6 years old, and 9% (range 6–14%) for children of 6–15 years. Paracetamol-related fatalities have gradually increased from an average of 7/year (range 4–10) in 2000–2005 to an average of 11/year (range 6–17) in 2010–2013, whereas the number of liver transplantations remained low, average 0.6/year (range 0–2). For patients in need of MARS-treatment a slight decrease was seen. Simultaneously, a pronounced increase in the sales of paracetamol from 5.6 (47% prescription, 53% OTC) to 29.7 (81% prescription, 19% OTC) DDD/1000 inhabitants/day from 2001 to 2014 is recorded. The best linear relationship ( $R^2=0.97$ ;  $p<0.001$ ) was observed between FPIC calls involving adults and prescription sales of paracetamol in 2001–2014. For fatalities and sales a weaker relationship is seen ( $R^2=0.317$ ;  $p=0.045$ ). Also the relationship between FPIC calls involving adults and paracetamol-related fatalities has a positive trend, although poorly described by a linear fit ( $R^2=0.352$ ;  $p=0.032$ ). **Conclusion:** The increase in FPIC queries are better explained by increased paracetamol sales rather than changes in the chosen indicators for serious poisonings. Although there is an evident trend between sales and fatalities the relationship remains weak, possibly due to the small number of fatalities.

### Reference

- [1] Höjer J, Karlson-Stiber C, Landgren A, et al. Paracetamol förgiftningar allt vanligare. *Läkaretidningen* 2013; 110:CFW3; [cited 2015 Nov 12]. Available at: <http://www.lakartidningen.se/Klinik-och-vetenskap/Rapport/2013/10/Paracetamolforgiftningar-allt-vanligare/#eng>

## 201. A 4-year analysis of calls answered by the staff at Red Cross War Memorial Children's Hospital (RCWMCH) Poisons Information Centre (PIC) in South Africa

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**Objective:** In South Africa information about exposure to poisonous substances is very limited.[1,2] To address this gap a study was undertaken to describe the experience of the poisons helpline at the RCWMCH PIC located in Cape Town, South Africa. **Methods:** A retrospective cross-sectional study of telephone calls to the RCWMCH PIC on human poison exposures during daytime working hours, from 20 January 2011 to 31 December 2014 was completed. Calls were recorded in AfriTox TeleLog, a purpose-designed database for collecting demographic, clinical and toxicological information from calls received by a poisons helpline. **Results:** Over the study period, 3896 calls relating to human poison exposures were received, involving 4279 agents or substances. Of all exposures, children <13 years were involved in 62%, adolescents (13–19 years) in 5%, and adults in 33%. The number of exposures remained relatively stable year on year. Of the nine provinces in South Africa, 79% of all calls came from those that include the major cities in South Africa, namely Gauteng, Kwazulu-Natal and the Western Cape. Ingestion was the most common route of exposure, accounting for 83% of cases. Most exposures were accidental (76%). Of these, 77.5% were children, 60% of whom were aged 1–2 years. Of the intentional exposures where gender was recorded, 55% of adults and 81% of adolescents were female. Ingestion of two or more substances accounted for 248 exposures. The majority of these multiple ingestions (60%) involved adults who had ingested pharmaceuticals in 72% of cases. Substances involved in all calls were predominantly pharmaceuticals (35.8%), pesticides and repellents (14.5%), and household products (13.7%). **Conclusion:** Six of the nine provinces in South Africa were underrepresented in the profile of calls received suggesting that improved surveillance is required in these predominantly rural provinces to gain a more comprehensive understanding of poisoning in the whole country. Since the majority of exposures involved children, consideration should be given to preventing these exposures by implementing legislation which encourages the wider use of child-resistant containers, appropriate storage and labelling of potentially harmful products.

### References

- [1] Balme K, Roberts JC, Glasstone M, et al. The changing trends of childhood poisoning at a tertiary children's hospital in South Africa. *S Afr Med J*. 2012;102:142–146.
- [2] Veale DJH, Wium CA, Müller GJ. Toxicovigilance I: a survey of acute poisonings in South Africa based on Tygerberg Poison Information Centre data. *S Afr Med J*. 2013;103:293–297.

## 202. Referrals from UK schools to the NPIS: an 8-year study

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**Objective:** Poisoning in children frequently occurs in the home, and is usually accidental and of low severity. Our objective was to analyse the frequency of poisonings occurring in UK schools. **Methods:** We retrospectively analysed all enquiries to the UK National Poisons Information Service (NPIS) involving children aged 4–19 years and originating from a school between January 2008 and May 2015. Calls were analysed with respect to gender, age, agent involved, poisoning severity and intent. **Results:** Over the study period, the UK NPIS received 1519 telephone enquiries regarding children with potential poisons exposure whilst at school. Males accounted for 60.4% of the total calls. Sixty-five percent of the calls involved secondary school-aged children (>12 years old). The agents encountered included low toxicity agents including poster paints and glue sticks (37%), pharmaceuticals (25%), chemicals used in science classes (20%) and plants (16%). Unknown agents, drugs of abuse and recreation accounted for the final 2%. Poisoning severity was graded “none” or “mild” (Poison Severity Score [PSS] 0 or 1) [1] for 95% of the calls received. Establishing intent was difficult. Accidental poisoning was common in all age groups. Deliberate self-poisoning accounted for a greater proportion of poisoning episodes in secondary school-aged children (0.5% in <12 versus 10.1% in >12), especially teenage girls, who accounted for 79.2% of the intentional poisonings. **Conclusion:** The UK NPIS receives around 200 enquiries per year originating from schools, the majority of which are accidental and of low severity. Consistent with published data, the proportion of exposures due to deliberate self-poisoning is higher in the teenage years, especially amongst girls.

### Reference

- [1] Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998;36:205–213.

## 203. Study of acute atypical antipsychotic poisonings in adults in Bulgaria

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**Objective:** The aim of the study was to analyze the epidemiologic features of atypical antipsychotics poisonings in adults in Bulgaria. **Methods:** Patients over 18 years of age with acute atypical antipsychotic poisonings hospitalized in the leading Clinic of Toxicology, Emergency University Hospital “N. I. Pirogov” for the period 2007–2014 were studied. Data were retrieved from the

medical documentation and were statistically analyzed. **Results:** There were 136 patients with atypical antipsychotic poisoning, which overall accounted for 6.2% of total medication poisonings ( $n = 2250$ ); it varied from 1.5% to 9.7% of all medication poisonings during the studied period. Conventional antipsychotics accounted for 5.3% ( $n = 119$ ) and varied from 9.96% to 2.87%. A tendency of increasing frequency of atypical antipsychotics poisonings and decreasing conventional antipsychotics poisonings was observed. The most frequent medication in atypical antipsychotic overdose was quetiapine. In 73 cases only one drug was taken (53.7%) and in 63 cases (46.3%) multiple drugs were taken. The average age of patients was 40 years (95% CI 36–43); 48 (35.3%) were male and 88 (64.71%) were female. A significant prevalence of women was demonstrated in patients over 40 ( $p = 0.001$ ). The most frequent reason for overdose was a suicide attempt (97.8%,  $n = 133$ ). In 30 (22.6%) cases the intentional overdose was serial. Most patients ( $n = 135$ , 99.3%) had psychiatric disorders and 125 (91.91%) were treated with atypical antipsychotics. Most of the patients (93.2%, 95% CI 88.9–97.6%) met the following criteria: psychiatric disorder, the poisoning was a result of intentional overdose and the overdosed medication had been prescribed for the patient’s psychiatric disorder. **Conclusion:** The study shows a tendency of increasing frequency of atypical antipsychotic poisonings in Bulgaria. Most patients had psychiatric disorders and intentionally overdosed on their own medications. To reduce the frequency of these poisonings it is necessary to prevent the suicidal attempts of patients with psychiatric disorders.

## 204. Epidemiology of cannabis poisoning: data from the toxicology laboratory of the Poison Control and Pharmacovigilance Centre of Morocco (2013–2015)

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**Objective:** To assess harm associated with cannabis use and to describe the epidemiological features of cannabis poisoning cases. **Methods:** We analysed the requests of urine detection of cannabis sent to the toxicology laboratory of the Poison Control and Pharmacovigilance Centre of Morocco (CAPM-LAB) from January 2013 to September 2015. The qualitative determination of 11-nor- $\Delta^9$ -tetrahydrocannabinol-9-carboxylic acid (11-nor- $\Delta^9$ -THC-9-COOH) in urine was performed by chromatographic rapid test (the cut-off level was 50 ng/mL or higher). The data included circumstances of poisoning, sex, age distribution and symptomatology of the positive cases. **Results:** In total 224 requests for urine detection of cannabis were received at CAPM-LAB, of these 54% of patients were positive for cannabis with an average age of  $21.1 \pm 6.8$  years old. The sex-ratio was 11 (110 males, 10 females). Most of the positive cases (80%) were chronic users and the requests for determination of cannabis were from the addiction centres in these cases. Acute accidental exposures occurred in six cases (patients age less than 13 years old). Acute overdose in addictive circumstance occurred in 16 cases (17–28 years old).



All acute poisoning cases required hospitalization because of neurological symptoms. In 19.8% of cases, patients were positive also for other drugs of abuse. No deaths were reported. **Conclusion:** Cannabis use is common in Morocco and affects young people. Although chronic users were most common, there were also cases of acute poisoning in children.

## 205. The burden of malicious poisoning in the Emergency Department

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**Objective:** Child abuse is a significant cause of preventable morbidity and mortality. The non-therapeutic administration of pharmaceuticals and use of other substances for parental neglect may represent a form of child maltreatment. The American Academy of Pediatrics guidelines do not mention malicious use of pharmaceuticals and non-pharmaceuticals in the initial evaluation of suspected abuse.[1] We evaluated the frequency of suspected malicious abuse in patients referred to the Emergency Department (ED) of Bambino Gesù Pediatric Hospital (OPBG). **Methods:** A retrospective analysis of all children <5 years of age referred to the ED from 2000 to 2015 with a diagnosis coded as "poison exposure". Criteria for possible malicious poisoning were (1) repetitiveness with a trend leading to a worsening of conditions; (2) reticent parents, medical history incompatible with clinical examination; incongruity between exposure and the reported event; (3) child's attitude depending on presence of caregiver or not during clinical examination; (4) children <1 years and 5–11 years; (5) a history of previous injuries; (6) additional risk factors: siblings with the same history (poisoning or injuries), massive doses of substances, multiple exposure, unusual or illegal drug exposure. **Results:** There were 779,314 ED visits over the study period and 1794 cases met the inclusion criteria (0.23% of total ED visits). Median age was 2.7 years. Of these cases, 111 patients (6.18%) had more than two visits to the ED. In this group, the reason for visits to the ED was coded each time as "poisoning" for 21 patients (18.9%) while for 12 patients (10.8%) it was coded as "poisoning" with a positive history of trauma in previous visits. Furthermore, of the 111 cases, 32 patients (28.8%) were from the same family. The most commonly ingested agents were cleaning products, personal care products, sedatives/hypnotics/antipsychotics, levothyroxine, cough and cold preparations, analgesics, tobacco and plants. **Conclusion:** Malicious use of pharmaceuticals and non-pharmaceuticals may represent an under-recognized form and/or component of child maltreatment.[2] It should be considered when multiple substances are involved, with recurrent episodes and when the history is inconsistent with the clinical picture.[3] Continued toxicosurveillance is essential for awareness of correlated dangers.

## References

- [1] Guidelines for the evaluation of sexual abuse of children: subject review. American Academy of Pediatrics Committee on Child Abuse and Neglect. *Pediatrics*. 1999;103:186–191.

- [2] Yin S. Malicious use of nonpharmaceuticals in children. *Child Abuse Negl*. 2011;35:924–929.
- [3] Calello DP, Henretig FM. Pediatric toxicology: specialized approach to the poisoned child. *Emerg Med Clin North Am*. 2014;32:29–52.

## 206. Costs of adult poisoned patients admitted to an adult emergency department of a tertiary hospital evaluated through a toxicovigilance program

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**Objective:** Toxicovigilance is the active process of identifying and evaluating the toxic risks existing in a community, and evaluating the measures taken to reduce or eliminate them.[1,2] Through a validated toxicovigilance program (SAT-HULP) we examined the characteristics of acute poisoning cases (APC) attending the Emergency Department (ED) of the Hospital Universitario La Paz (HULP, Madrid, Spain) and assessed their economic impact on the health system.[3] **Methods:** An active poisoning surveillance system performs a daily search for cases in the hospital's computerized case records. Cases retrieved are entered into a database for recording of type of poisoning episode, reasons for exposure, causative agent, signs and symptoms, and treatment. We carried out a cross-sectional epidemiological study with analytical projection, based on an impact study on costs and cost per survivor. The data for the costs attributable to APC observed at HULP (outpatients and inpatients) was based on the information provided by the diagnosis-related groups (DRG) through the corresponding hospital discharge reports (available through SAT-HULP).[4] **Results:** During the first 3 years of SALT-HULP operation we found a total of 3750 APC, a cumulative incidence rate of 1.75% of patients attending the ED. The mean (SD) patient age was 40.9 (17.8) years and 51.2% were male. Drug abuse accounted for 51.7% of the cases and overdose of pharmaceutical agents for 34.8%. Suicide attempts were the second most frequent category (38.1%) and other causes accounted for 14.5% of APC. The total cost of hospital care for our hospital rose to €1,825,263.24 (approximately €730,105.30/year) resulting in a permanent occupation of 4 beds/year. **Conclusion:** SAT-HULP constitutes a validated toxicovigilance tool, which continuously integrates available data sources in real-time and helps health services manage APC data flexibly, including the consumption of resources from the health system.

## References

- [1] World Health Organisation. Poisoning prevention and management 2011; [cited 2015 Nov 15]. Available at: [www.who.int/pcs/poisons/en](http://www.who.int/pcs/poisons/en)
- [2] Watson AW, Litovitz T, Belson MG, et al. The Toxic Exposure Surveillance System (TESS): risk assessment and real-time toxicovigilance across USA poison centers. *Toxicol Appl Pharmacol*. 2005;207:604–610.
- [3] Muñoz R, Borobia A, Qunitana M, et al. Desarrollo y validación de un programa de toxicovigilancia con detección automatizada de casos en un hospital terciario (SAT-HULP). *Emergencias*. 2013;25:423–429.

- [4] Yang CM, Reinke W. Feasibility and validity of International Classification of Diseases based case-mix indices. *BMC Health Serv Res.* 2006;6:125.

## 207. Characterization of marijuana use in US college students as reported to an online survey

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**Objective:** Although marijuana is a federally controlled substance, half of US states have passed medical marijuana legislation and several have legalized recreational marijuana.[1,2] Overconsumption of edible products has been associated with increased emergency department visits and blamed in adult deaths. Our objective was to describe marijuana use among US college students. **Methods:** The RADARS<sup>®</sup> System College Survey Program is an online questionnaire of students attending a 2 or 4 year university, technical or online school to assess non-medical use of prescription drugs. Surveys are administered to different students during the fall, spring and summer semesters across the US. Questions about marijuana use/accessibility/risk were added in the 2014 through the 2015 spring semester surveys. States were categorized as non-legal, medical or medical + recreational based on decriminalization/legalization status during the study period. **Results:** Overall 7105 respondents were included: 4404 were from non-legal, 2482 from medical, and 219 from medical + recreational states (Table 1). In non-legal states 10% of students reported purchasing marijuana in a store. Respondents stated it was easy to obtain with increasing frequency from non-legal (81%) to medical (83%) to medical + recreational (87%) ( $p = 0.02$ ). Regardless of marijuana legislation, slightly less than half perceived marijuana use to be a great-moderate risk to mental health ( $p = 0.12$ ). **Conclusion:** Recreational marijuana legalization is associated with increased use, increased edible consumption and easy access for college students. Standardization of edible product manufacturing may be needed to reduce morbidity, particularly as its frequency is increasing. Students in non-legal states purchased marijuana in stores suggesting diversion from medical and medical + recreational states to non-legal states. Continued surveillance is necessary to determine the long-term impact (e.g. academic performance, driving while impaired) on use among college students.

**Table 1.** Characteristics of students who indicated they used marijuana during the last 3 months.

Characteristics of students	Status of marijuana based on decriminalization/legalization status during the study period			p value
	Non-legal	Medical	Medical+ Recreational	
Used marijuana (%)	950 (22)	630 (25)	62 (28)	<0.001
Median age in years (IQR)	24 (21, 28)	24 (21, 29)	24 (22, 27)	0.59
Median days of use (IQR)	5 (2, 20)	6 (2, 20)	10 (2, 25)	0.58
Smoked (%)	845 (89)	545 (87)	54 (87)	0.34
Ingested edible (%)	241 (25)	200 (32)	29 (37)	<0.001
Vaporize/e-cigarette (%)	247 (26)	167 (27)	14 (23)	0.80

## References

- [1] Johnston LD, O'Malley PM, Miech RA, et al. Key findings on adolescent drug use; [cited 2014 Nov 15]. Available at: <http://www.monitoringthefuture.org/pubs/monographs/mtf-overview2014.pdf>
- [2] Choo EK, Benz M, Zaller N, et al. The impact of state medical marijuana legislation on adolescent marijuana use. *J Adolesc Health.* 2014;55:160–166.

## 208. Severe and fatal accidental pharmaceutical poisoning in young children in the UK

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**Objective:** Accidental pharmaceutical poisoning in young children is common, but severe or fatal events are rare. This study was performed to identify the number of such events occurring in the UK and the medications that were most commonly responsible. **Methods:** Data, with identification of causative agent where possible, were obtained from the Office of National Statistics (ONS) for fatal poisoning and the Paediatric Intensive Care Audit Network (PICANet) and the National Poisons Information Service (NPIS) for severe non-fatal poisoning. English hospital admission and prescribing data for implicated agents were obtained from Hospital Episode Statistics (HES) and the electronic Prescribing Analysis and Cost (ePACT) databases, respectively. **Results:** Between 2001 and 2013 there were 28 children aged under 5 years with a death registered as due to accidental poisoning by a pharmaceutical product in England and Wales. Methadone was the causative drug in 16 cases and tricyclic antidepressants in 3. Deaths per million primary care prescriptions were substantially higher for methadone (0.58) than tricyclic antidepressants (0.02), the next most common drug group causing childhood deaths. In the UK 201 children aged under 5 years were admitted to paediatric intensive care with pharmaceutical poisoning between 2002 and 2012. The agent responsible was identified in 115 cases, most commonly benzodiazepines (22 cases), methadone (20 cases), other opioids (19 cases) and tricyclic antidepressants (13 cases). It was often not possible to differentiate between poisoning due to exploratory ingestion and iatrogenic causes. Iron and its products, anticonvulsants and methadone were the most common agents reported to NPIS with severe symptoms associated with ingestion in young children. For children aged under 14 years, hospital episode statistics demonstrate a fall in admissions due to poisoning by the drug groups associated with deaths in the early 2000s with a steady rate since 2006. **Conclusion:** Methadone is the most common pharmaceutical causing fatal poisoning and a common cause of intensive care admissions in young children in the UK. Further measures to reinforce safe storage and use in the home, including considering pharmacy supervised therapy for parents who are on opiate replacement therapy, might lead to a significant reduction in deaths. A robust system for reporting significant harm associated with accidental poisoning in the UK would assist further targeted prevention strategies for other implicated medications and help with the early identification of other potentially toxic substances.

## 209. Copper sulphate experiments: an unnecessary hazard at school

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**Objective:** In Danish schools pupils carry out experiments with copper sulphate in science lessons in order to learn about the formation of salt crystals. Copper sulphate can be corrosive to the skin and eyes, and oral exposure often results in intense nausea, vomiting and diarrhea. Human death has been reported after ingestion of gram quantities of this material; the LD<sub>50</sub> (oral) for copper sulphate is 300 mg/kg in rats.[1] The objective of this study was to identify the extent of copper sulphate exposure at Danish schools in order to prevent serious harm. **Methods:** A retrospective study based on the systematic registration of enquiries to the Danish Poisons Information Centre (DPIC) regarding exposure to copper sulphate. The observation period was January 2007 to October 2015; all registrations on the cases, including poisoning severity grading, were performed systematically and immediately following the call. **Results:** In total 156 cases were collected; there were 11–28 cases/year. The majority of patients were of school age 11–15 years ( $n=94$ ); median age was 14 years (range 0–80 years). Most exposures occurred in school ( $n=104$ ). The majority of exposures were accidental ( $n=144$ ) and/or by play ( $n=38$ ). The most common routes of exposure were eye ( $n=56$ ) and oral ( $n=52$ ), followed by inhalation ( $n=33$ ) and dermal exposure ( $n=13$ ). Eye exposure caused irritation, burning pain and redness; oral exposure caused mucosal irritation, gastric pain, nausea and vomiting. Inhalation of copper sulphate vapour and dust caused headache, vertigo and general discomfort. The risk assessment of cases was as follows: no risk ( $n=31$ ), mild risk ( $n=45$ ), moderate risk ( $n=73$ ) and severe risk ( $n=2$ ). In total 46% of the patients were recommended for further examination at a healthcare facility. **Conclusion:** On average the DPIC received a call once a month concerning accidental exposure of school pupils to copper sulphate. Although there have been no fatalities, we think that exposure to this potent chemical should be prevented by avoiding the use of it in the classrooms e.g. by substituting it with a less harmful chemical.

### Reference

- [1] Copper sulfate. POISINDEX<sup>®</sup> System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA; [cited 2016 Nov 6]. Available at: <http://www.micromedexsolutions.com/>

## 210. Toxic love: a 3-year retrospective analysis of love-related toxicological deliberate self-harm

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**Objective:** Suicide is the 10th cause of death in US, among which self-poisoning is the 3th cause (2.1/100.000 population).[1] Deliberate self-harm (DHS) poisoning for attempting suicide accounted for 10.5% of queries to US Poison Centers and 31.7% of all fatalities [2] in 2013. In our experience, relationship problems are an important cause for toxicological DHS. Our aim was to investigate epidemiological, demographic and clinical aspects of love-related DHS. **Methods:** Patients admitted to the Toxicological Unit of Florence Careggi University Hospital from 2012 to 2014 with DHS by poisoning diagnosis (8.9% of acute intoxications) were studied. We analyzed clinical records, including psychiatric evaluation when available. Patients without psychiatric evaluation, essential for pinpointing the cause(s) and themes of attempted suicide, were excluded. **Results:** There were 252 patients in which psychiatric evaluation was performed in 157 (62.3%). Love-related DHS poisonings numbered 39 (24.8%). The average age was 42.9 years (16–78 years) with male/female ratio of 1 to 2.6. The agents involved were drugs (87%), caustics (8%) and inhalation of carbon monoxide (5%). Drugs cohort was divided in the following categories: single psychoactive drug (59.3%), mixed psychoactive drugs (31.5%), non-psychoactive drugs (12.5%), mixed psychoactive and other drugs (9.1%). The average hospitalization period was 3.9 days (1 to 22 days). All patients survived without sequelae. The psychological factors reported were: pure disappointed love (28.2%), disappointed relationship as contributory or precipitating cause (25.6%), separation or divorce (20.5%), violence or abuse (12.8%), partner abandonment (7.6%) and death of partner (5.1%). It was sometimes difficult, also for the psychiatrist, to distinguish between genuine or simulated attempted suicide; however the first one usually has aspects of “planned escape” such as identification of next of kin or official contact, leaving written instructions for funeral, bequests and caring for help/support for someone else. **Conclusion:** Love-related DHS is an important cause of poisoning. The psychiatrist should investigate the patient’s biological and psychopathological triggers for suicidal ideation. Love is deeply biological and a “broken heart” or a failed relationship can have disastrous effects. However, without loving relationships, humans fail to flourish, even if all of their other basic needs are met.

### References

- [1] Suicide. Facts at a glance [cited 2015 nov 21]. Available at: <http://www.cdc.gov/violenceprevention/pdf/suicide-datasheet-a.pdf>
- [2] Mowry JB, Spyker DA, Cantilena LR Jr, et al. 2013 Annual Report of the American Association of Poison Control Centers’ National Poison Data System (NPDS): 31st Annual Report. *Clin Toxicol (Phila)*. 2014;52:1032–1283.

## 211. Native British snake bites in the UK: an estimation of occurrence and antivenom usage

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**Objective:** Little is known about the use of antivenom for *Vipera berus* envenoming in the UK. There is no central data collection

of bites or antivenom use. We aimed to estimate the number of bites and antivenom administrations from telephone enquiries and TOXBASE<sup>®</sup> accesses. **Methods:** Telephone enquiries and TOXBASE<sup>®</sup> accesses relating to European Viper Antivenom or *Vipera berus* bites received between 1 January 2013 and 30 September 2015 were cross-referenced by time and place and grouped in order to identify cases. Cases were identified from telephone enquiries and potential cases identified from TOXBASE<sup>®</sup> accesses that occurred outside of 48 hours from a previous enquiry/access from a user with the same postcode. A time frame of 48 hours was used as only a small number of cases occur and current advice recommends all patients who have been bitten are observed for 24 hours. **Results:** There were 106 cases (171 telephone enquiries) over the study period; for 29 cases no matching TOXBASE<sup>®</sup> accesses identified. There were 1574 TOXBASE<sup>®</sup> user accesses to the snake entry and 542 to the antivenom entry. After cross-referencing all accesses and telephone enquiries there were 1316 potential cases identified, including 273 cases (310 accesses) where the user only accessed the antivenom entry, these cases were excluded. Antivenom was used in 50 cases identified in telephone enquiries (TOXBASE<sup>®</sup> criteria for antivenom administration met in all cases) and a further 132 possible cases identified from the access data (user looked at both snake and antivenom entries). **Conclusion:** The number of *Vipera berus* cases presenting to healthcare facilities in the UK is very low, estimated to be 0.06–0.6/100,000 population/year; [1] antivenom administrations are estimated to be 0.03–0.1/100,000 population/year. [1] These may be underestimates as clinicians may administer antivenom without TOXBASE<sup>®</sup> guidance; however, it is routine to use TOXBASE<sup>®</sup> for poisoned or envenomed patients presenting to hospital in the UK. In addition 273 antivenom only cases were excluded since users may have been looking to locate antivenom as per the current National Poisons Information Service (NPIS)/College of Emergency Medicine (CEM) recommendations. If these estimations are representative, the current recommendation for all emergency departments to stock two vials of antivenom should be reconsidered in view of the low rate of use and the increased costs of currently available licensed antivenoms. Additional vials should be made available within a few hours.

## Reference

- [1] Annual Mid-year Population Estimates: 2014; [cited 2015 Nov 26]. Available at: <http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk-england-and-wales-scotland-and-northern-ireland/mid-2014/stb—mid-2014-uk-population-estimates.html>

## 212. Iron poisoning and the use of desferrioxamine: survey data from the UK National Poisons Information Service (NPIS)

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**Objective:** To assess the incidence and severity of iron poisoning cases referred by hospitals to the UK NPIS and the use of desferrioxamine. **Methods:** Data were collected prospectively on patients presenting to hospital between 1 July 2014 and 20 September 2015. Inclusion criteria were: ingestion of a potentially toxic dose of iron ( $\geq 20$  mg/kg); patient symptomatic; raised serum iron concentration (greater than or  $\geq 55$   $\mu\text{mol/L}$ ); or patient being treated with desferrioxamine. **Results:** Over 14.5 months, 319 cases were referred to NPIS; 26 patients did not meet follow up criteria and were excluded. Patients fulfilled at least one criterion as follows: toxic dose 111/293 (143 no data; 39 < 20 mg/kg); symptomatic patient 184/293; serum iron  $\geq 55$   $\mu\text{mol/L}$  128/293 (94 no data; 72 < 55  $\mu\text{mol/L}$ ); received desferrioxamine: 29/293 (including 2 requests for information on formulation). Overall 37.2% of patients were asymptomatic, 49.1%, 9.2%, and 3.1% had minor (Poisoning Severity Score [PSS] 1), moderate (PSS 2) and severe (PSS 3) features, respectively; 1.4% had unknown severity. One third of cases (34.7%) were mixed overdoses. Elemental iron dose reported to be ingested ranged from 3.76–313 mg/kg. The amount of elemental iron ingested did not correlate with PSS at the time of the call or with plasma iron concentrations (at 3.5–4.5 h or 5.5–6.5 h). However, there was a correlation between plasma iron concentration at 3.5–4.5 h and PSS. Of the 29 patients treated with desferrioxamine, 13.8% were asymptomatic, while 44.8%, 13.8% and 3.4% of patients were PSS 1, PSS 2 or PSS 3, respectively. Features reported included acidosis ( $n = 12$ ), haematemesis ( $n = 5$ ), hypotension ( $n = 4$ , including 2 mixed ingestions) and drowsiness ( $n = 2$  patients, both mixed ingestions). Fourteen patients received doses similar to standard recommendations (15 mg/kg/h up to a dose of 80 mg/kg; total dose given 60–83 mg/kg). Six patients were treated with other doses or details were unknown. Two enquiries were requests for pharmacy advice while one related to a treatment error. In six cases treatment discontinuation was advised due to the absence of severe features and/or elevated plasma iron concentration. No adverse events/reactions to desferrioxamine were noted. **Conclusion:** We obtained information on 293 cases with potentially significant iron poisoning from telephone calls to the NPIS. Reported dose of elemental iron ingested did not predict either poisoning severity or plasma iron concentrations; however, plasma concentrations at 3.5–4.5 hours post-ingestion did correlate with PSS. Few patients had poisoning significant enough to require treatment with desferrioxamine.

## 213. Toxicity of 2,4 dinitrophenol: impact of public health measures discouraging use on episodes of toxicity referred to the UK National Poisons Information Service

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**Objective:** 2,4-Dinitrophenol (DNP) is used as a weight losing and “fat burning” drug but may cause severe and sometimes fatal toxicity.[1] Following an increase in cases reported to the UK

National Poisons Information Service (NPIS) between 2010 and 2013,[2] public health measures were taken in late 2013 and early 2014 to reduce use. These included publication of warnings, educational work in gyms and a crackdown on illegal sales. This study was performed to assess the impact of these measures on presentations with toxicity relating to DNP reported to the NPIS. **Methods:** NPIS telephone enquiry records and user sessions for TOXBASE<sup>®</sup>, the NPIS online information database, involving systemic exposures to DNP, were reviewed for the period 1 January 2007 to 17 September 2015. **Results:** There were 29 individual cases of DNP toxicity reported between 2007 and 2013, 5 of which had a fatal outcome, with 21 cases and 3 deaths occurring in 2013. Following public health measures there was a reduction in reported episodes, with 9 cases reported throughout 2014. However, referrals to NPIS subsequently increased sharply, with 30 cases referred between 1 January and 17 September 2015, five resulting in death. Most of those affected were teenagers and younger adults. Between 2007 and 2013 few cases were female (3/29), but the proportion of females involved in 2014 and 2015 increased substantially (22/39,  $P < 0.001$ ). Accesses to the DNP page on TOXBASE<sup>®</sup> also reduced during 2014 but increased again in 2015. **Conclusion:** Public health measures taken in the UK reduced the number of exposures with DNP reported to the NPIS, but this effect was short-lived and exposures are now more common in the UK than ever before and increasingly involve females. Further steps are required to reduce consumption and cases of poisoning with DNP.

## References

- [1] Grundlingh J, Dargan P, El-Zanfaly M, et al. 2,4-Dinitrophenol (DNP): a weight loss agent with significant acute toxicity and risk of death. *J Med Toxicol.* 2011;7:205–212.
- [2] Kamour A, George N, Gwynnette D, et al. Increasing frequency of severe clinical toxicity after use of 2,4-dinitrophenol in the UK. A report from the National Poisons Information Service. *Emerg Med J.* 2015;32:383–386.

## 215. Caffeine-containing energy drinks and caffeine poisoning in school-age children (5–16 years): TOXBASE<sup>®</sup> access and enquiry data

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**Objective:** To assess the incidence of poisoning with caffeine-containing energy drinks in the UK, particularly in school-age children and adolescents (5–16 years), by studying accesses to TOXBASE<sup>®</sup> (the UK's National Poisons Information Service [NPIS] poisons management database) and telephone enquiries to the NPIS (recorded on the UK's Poisons Information Database [UKPID]). **Methods:** We identified the number of TOXBASE<sup>®</sup> accesses to all products containing caffeine and to caffeine-containing energy drinks and identified relevant NPIS telephone enquiries using the search terms “caffeine” and “energy drink” (along with caffeine as

an ingredient) together with the brand names of 13 specific energy drinks. The period studied was 1 January 2009 to 31 July 2015. **Results:** TOXBASE<sup>®</sup> accesses to the caffeine entry steadily increased from around 1000 in 2009 to some 2200 in 2014. Accesses to energy drink entries remained constant at around 200–250/year. Accesses to energy drinks accounted for 2–5% of all accesses to caffeine-containing products. A total of 4754 telephone calls were received where “caffeine” or “energy drink” was the agent or ingredient. One-hundred and sixteen enquiries (2.4%) related to the ingestion of caffeine-containing energy drinks alone. Fifty-two patients were asymptomatic (45%); 55 (47%) presented with minor features (Poisoning Severity Score [PSS] 1) and 7 (6%) patients developed moderate (PSS 2) features. There were no severe or fatal exposures reported. Commonly reported features were agitation (7%), vomiting, tachycardia, palpitations (6% each) and abdominal pain (5%). Thirty-five of 116 (30%) calls related to school-age children (5–16 years). Fourteen patients were reported as asymptomatic (40%); 19 (54%) presented with minor (PSS 1) and 2 (6%) with moderate (PSS 2) features. In this age group, the most commonly reported features were: agitation (14%); tachycardia, headache (11% each); vomiting and mydriasis (9% each). **Conclusion:** Accesses to the TOXBASE<sup>®</sup> entry for caffeine have steadily increased over the last 6 years, but there was no corresponding increase in accesses to entries for caffeine-containing energy drinks. It is possible that treating clinicians are aware that toxicity is related to the caffeine content and are viewing the caffeine entry directly. There were few calls which related to single ingestions of caffeine-containing energy drinks and even fewer of these related to ingestions in school-age children. In the majority of cases discussed with the NPIS, patients were asymptomatic or presented with minor features; the incidence of moderate adverse effects was low and no cases of severe poisoning were reported.

## 216. Fatal poisonings: a 5-year case series of the Pavia Poison Centre

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**Objective:** According to the WHO, 346,000 deaths due to accidental poisoning occurred worldwide in 2004. Moreover, almost a million people die every year as a result of suicide and, among these, the deliberate ingestion of pesticides causes about 370,000 deaths/year.[1] We describe fatal intoxications in the case series of the Pavia Poison Centre (PPC). **Methods:** A retrospective review of fatal poisonings managed by the PCC from 2010 to 2014 was performed. The included cases were assessed for age, sex, modality and route of intoxication, PSS (Poisoning Severity Score) at the first consultation with the PPC and agents involved. Cases for which the cause-effect relationship between exposure and death was considered absent or unlikely by the specialist toxicologist were excluded. **Results:** In the study period, 239 fatal cases were included (50% males, 60 ± 20 years), distributed all over Italy, with an average of 47 deaths/year. Five patients (5/239; 2%) were younger than 14 years, and fifty patients (50/239, 21%) were older than 78 years. The exposure was considered accidental in 46 cases (19%), voluntary in 103 cases (42%) with 34 cases of suicide, and related to an adverse drugs reaction in 59 cases (25%). In 31 cases (14%) this data was unknown. Among the cases of suicide, 41.5% of patients were aged between 36 and 56 years. Ingestion

was the route of exposure in 80% of cases (191/239). Seventy-five percent of patients (179/239) presented a serious clinical picture at the first PPC consultation (PSS 3). Concerning the agents involved, drugs were the cause of death in 110 cases (46%). Among these, the death was related to the ingestion of only one drug in 65 cases (59%), and metformin was involved in more than half of these (35/65). In 18% of cases (42/110) more than one agent was involved. Other agents involved in more than 15 cases were caustics (7.5%), pesticides (7.5%), drugs of abuse (7%), gas/smoke/fire inhalation (7%) and mushrooms (5%). **Conclusion:** Fatal poisonings are not related only to suicide, but also to adverse drug reactions and accidental ingestions. The role of poison centers is crucial in identifying the main causes and modality of lethal intoxications, and in reporting alerts to the authorities in order to identify possible preventive interventions.

## Reference

- [1] World Health Organization. The global burden of disease: 2004 update; [cited 2015 Nov 20]. Available at: [http://www.who.int/healthinfo/global\\_burden\\_disease/GBD\\_report\\_2004update\\_full.pdf](http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf)

## 217. Poisonings in children under 18 years of age presenting to the Emergency Department, Landspítali University Hospital, Iceland

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**Objective:** To examine the incidence and nature of poisonings in children presenting to the Emergency Department (ED) at Landspítali University Hospital in 2012, and to compare the rate to the average rate of poisonings in all age groups presenting to the ED the same year, 3.1 cases per 1000 inhabitants.[1] **Methods:** The study was prospective and included all visits due to poisonings in children and adolescents under 18 years of age during 2012. Information collected included age and gender of each patient, location and causes of the poisoning, type and amount of poison, route of exposure, clinical manifestations, treatment and outcome. **Results:** In 2012, 166 children came to the ED because of poisoning, 102 girls and 64 boys. That represents a rate of 2.2 per 1000 inhabitants in this age group in Iceland. Ingestion was the most common route of exposure (79%) and the patient's home was the most common location of exposure. In children aged 0–12 years 98% of the poisonings were unintentional but in the age group 13–17 years 80% were deliberate. Drugs and/or alcohol were involved in 66% of cases. The most common group of drugs was selective serotonin re-uptake inhibitors (SSRIs) and the most common single drug was paracetamol. Alcohol was involved in 26% of cases in the 13–17 years old but only in one case in children under 13 years of age. The most common household product exposure was to detergents. The majority of the children were treated in the ED and discharged home within 24 hours; 28 children (17%) were admitted to other departments of the hospital for further treatment. No deaths occurred. **Conclusion:** The rate of poisonings in children presenting to the ED in 2012 is lower than the average rate per 1000 inhabitants. Girls outnumbered boys. The nature of poisonings in children varies in different age groups. Accidental unintentional poisonings are most common in younger children up to 12 years old whereas self-poisonings by ingestion of prescription drugs

and/or alcohol accounted for the majority of cases in the older group.

## Reference

- [1] Gudjonsdottir GA, Thordardottir AM, Kristinsson J. Acute poisonings in Iceland: A prospective study on poisonings presenting to the Emergency Department at Landspítali University Hospital. *Clin Toxicol (Phila)*. 2014;52:312.

## 219. Alcohol-based hand sanitizer exposure: characterization and comparison of US National Poison Data System (NPDS) data and a 5-state regional poison center from 2010–2014

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**Objective:** To characterize alcohol-based hand sanitizer human exposures within our 5-state Regional US Poison Center (RPC) and compare our findings to national data. **Methods:** We reviewed all National Poison Data System (NPDS) data coded for ethanol-based and isopropanol-based hand sanitizer human exposures from 2010–2014 within our 5-state RPC and compared it to the national data. Parameters evaluated were age, gender, route, reason for exposure, clinical effects, level of healthcare facility (HCF) care, management site, medical outcome, and therapies. **Results:** Nationally, NPDS reported 78,781 exposures to alcohol-based hand sanitizers over the study period; 38,485 (48.9%) were female. Most were oral exposures (93%, 73,643), followed by ocular (5.9%) and dermal (3.8%) routes. The most common reason for exposure was accidental (92%, 72,495) with 4889 (6.2%) exposures deemed as intentional. From 2010 to 2014, the number of intentional misuse or abuse calls rose each year. Ages ranged from 2 days old to 104 years old. Overall 21,118 patients (26.8%) had no effects, 6242 (7.9%) had minor effects, 874 (1.1%) had moderate effects, and 72 (0.1%) had major effects. Outcomes were unknown for 49,530 (62.9%) of exposures. There were 3 reported deaths during the 5-year period. The top 5 clinical effects reported were, respectively, ocular irritation, vomiting, drowsiness/lethargy, nausea, and coughing/choking. Most exposures (87.8%, 69,206) were managed on site (non-HCF). Our RPC reported 2840 human exposures to alcohol-based hand sanitizers during that same period; 1394 (49%) were female. Again most exposures were oral (93%, 2645), followed by ocular (6%) and dermal (1.4%). The most common reason for exposure was accidental (91.5%, 2599) with 188 (6.6%) deemed as intentional. The trend of abuse rose from 2010 to 2014. Ages ranged from 3 days old to 98 years old. Most patients (78.6%, 2232) had no effects, 430 (15%) had minor effects, and 30 (1%) had moderate effects. There were no major outcomes or deaths reported. Outcomes were unknown for 110 (3.9%) of exposures. Top 5 clinical effects were, respectively, dermal irritation, vomiting, drowsiness, oral irritation, and nausea. Most patients (90.8%, 2578) were managed on site (non-HCF). **Conclusion:** Alcohol-based hand sanitizer exposure is a common occurrence in the US. Most cases involve accidental ingestion scenarios and most cases resolve with minor symptomatology without requiring emergency medical attention. National data results were very consistent with the numbers at our RPC. Abuse/misuse was a small percentage of cases, but we suspect the rising trend will continue.

## 220. The effect of holidays on acute poisoning enquiries to the Danish Poison Information Centre

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**Objective:** Previous reports have shown that the number of contacts to the emergency departments due to poisonings declines during holidays.<sup>[1,2]</sup> However, this has not been examined from the perspective of poison centres which are usually the first point of contact. The aim of the study was to characterize the effects of holidays on enquiries to the Danish Poison Information Centre. **Methods:** We extracted all enquiries concerning acute poisonings from the Danish Poison Information Centre Database from 2008 to October 2015. The mean number of calls was calculated for school holidays, bank holidays, school days and weekends stratified for age, risk assessment, time of day, type of poisoning, and place. School days were used as the reference for comparisons. **Results:** We identified 107,838 enquiries regarding acute poisoning over the study period. During holidays, the number of calls per day increased by 9.7% from 36.6 to 40.1 enquiries/day. The increase was only seen during school holidays with a 12.5% increase while a 7.8% decrease was seen during bank holidays. Enquiries about children aged 0–4 years old predominantly contributed to the increase during school holidays with a 33.7% increase. The main increase in enquiries was during the time period from 9 am to 3 pm. The proportion of potentially life-threatening poisonings decreased slightly during school holidays from 5.4% to 5.0% of all calls. In the elderly (over 65 years of age), an increase in calls concerning medication errors was noted during bank holidays accounting for 41.7% of the calls compared to 27.8% of the calls during school days. **Conclusion:** In contrast to previous reports, we saw an increase in the number of calls during school holidays, mainly concerning younger children (below 5 years of age).<sup>[1,2]</sup> A possible explanation could be that the daytime child care for the vast majority of pre-school children in Denmark are daytime nursery or nursery schools which has a lower risk of accidental poisoning.

### References

- [1] Hughes K, McHale P, Wyke S, et al. Child injury: using national emergency department monitoring systems to identify temporal and demographic risk factors. *Inj Prev.* 2014;20:74–80.
- [2] Chien C, Marriott JL, Ashby K, et al. Unintentional ingestion of over the counter medications in children less than 5 years old. *J Paediatr Child Health.* 2003;39:264–269.

## 221. Tracking the trends over time of unintentional pediatric exposures to benzodiazepines and opioids reported to poison centres in the Global Toxicosurveillance Network

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**Objective:** To determine if population rates of unintentional pediatric human exposures for benzodiazepines are experiencing similar trends as those of opioid exposures as reported to poison centres (PCs) in France, Germany, Italy, the UK, and the US. **Methods:** Unintentional pediatric exposures to benzodiazepines (alprazolam, diazepam, etizolam, flunitrazepam, lorazepam, lormetazepam, nitrazepam, oxazepam, phenazepam, temazepam) and opioids (buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, pethidine, tramadol) reported to Global Toxicosurveillance Network (GTNet) PCs were examined to observe trend similarities. Unintentional pediatric (<6 years) exposures occurring from 2012–2014 were obtained from PCs in Paris (France), Göttingen (Germany), Milan (Italy), the UK (4 sites), and the US. UK PCs provide medical management assistance to healthcare providers only, while services in all other countries are also available to the public. Defined regions of call coverage exist in the Paris, Göttingen, UK, and US sites, while Milan handles 65–70% of calls in Italy. Rates are expressed as the number of unintentional pediatric exposures per 100,000 population. Poisson regression was used to determine differences in rate changes between benzodiazepine and opioid exposures with both discrete and continuous covariates. An analysis of covariance test determined differences between the overall rates changes over time for benzodiazepine and opioid exposures. **Results:** For unintentional pediatric exposures, benzodiazepine exposure rates were higher than opioid exposures in Germany, Italy, and the US, while opioid exposure rates were consistently higher than benzodiazepines in the UK. Benzodiazepine exposure rates decreased in all countries (statistically significant decreases only in the US [ $p=0.0038$ ]). Similar decreases over time in opioid exposure rates were observed in Germany and the US. The negative slopes for benzodiazepine and opioid exposures within these two countries did not significantly differ. In contrast, France, Italy, and the UK experienced overall increases of opioid exposures. An analysis of covariates identified a statistically significant difference between the negative slope of exposure rates for benzodiazepines and the positive slope of opioid exposures in France ( $p=0.0455$ ), though variability exists across quarters. **Conclusion:** Decreases over time in unintentional pediatric exposure rates for both benzodiazepines and opioids were observed in Germany and the US only. Benzodiazepine and opioid exposure rates have not experienced similar directional trends in France, Italy, or the UK. Despite decreases over time, further research is warranted to elaborate on the identification that unintentional pediatric exposure rates of benzodiazepines are often higher than those of opioids.

## 222. Tracking the trends over time of global adult human exposures to benzodiazepines and opioids reported to poison centres in the Global Toxicsurveillance Network

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**Objective:** To determine if rates of adult human exposures for benzodiazepines are experiencing similar patterns over time as for opioid exposures reported to poison centres (PCs) in France, Germany, Italy, the UK and the US. **Methods:** Human exposures to benzodiazepines (alprazolam, diazepam, etizolam, flunitrazepam, lorazepam, lormetazepam, nitrazepam, oxazepam, phenazepam, temazepam) and opioids (buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, pethidine, tramadol) reported to Global Toxicsurveillance Network (GTNet) PCs were examined to observe trend similarities. Adult ( $\geq 18$  years) human exposures occurring from 2012–2014 were obtained from PCs in Paris (France), Göttingen (Germany), Milan (Italy), the UK (4 sites), and the US. UK PCs provide medical management assistance to healthcare providers only, while services in other participating countries are also available to the public. Defined regions of call coverage exist for the Paris, Göttingen, UK, and US sites, while Milan handles 65–70% of calls in Italy. Rates are expressed as the number of exposures per 100,000 population (extrapolated from country census data) separately for total, all intentional, and all unintentional exposures. Poisson regression was used to determine differences in rate change between benzodiazepines and opioids with both discrete and continuous covariates. **Results:** Intentional benzodiazepine exposure rates were consistently higher than opioid exposure rates in each country. The magnitude of difference between rates of benzodiazepine and opioid exposures appeared greater for intentional exposures than unintentional exposures in each country. For total exposures, overall decreases exist for both benzodiazepines and opioids in France, Germany, the UK, and the US. Within these countries, the decreasing slopes of benzodiazepine and opioid exposures did not differ significantly from each other. An analysis of covariance identified a statistically significant difference between the slopes of total exposure rates for benzodiazepines and opioids ( $p = 0.0226$ ) only in Italy, where opioid exposures increased over time ( $p = 0.0571$ ) and significantly decreased for benzodiazepines ( $p = 0.0134$ ). Overall decreases in intentional benzodiazepine exposures were observed in all countries. Overall decreases in intentional opioid exposures were similarly observed in all countries except Italy, where exposures increased. The difference between intentional benzodiazepine and opioid slopes was not significant in any country. **Conclusion:** As benzodiazepine exposures (both total and intentional) decreased overall in France, Germany, the UK,

and the US, a similar decrease was observed for opioid exposures in these countries. The only statistically significant difference between rate change slopes exists in Italy, where total exposures to benzodiazepines decreased and total exposures to opioids increased.

## 223. Carbamazepine enquiries to the National Poisons Information Centre of Ireland: a prospective 7 year study

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**Objective:** To characterise the epidemiology of carbamazepine enquiries to the National Poisons Information Centre (NPIC) Dublin. **Methods:** This study prospectively examined all enquiries involving carbamazepine reported to the NPIC from 1 May 2006 to 30 April 2013. Variables collated included age, sex, intent, location of incident, severity and symptoms. **Results:** During the 7 year study period there were 256 enquiries relating to 222 patients; 51.4% ( $n = 114$ ) were females, 47.7% ( $n = 106$ ) were males and gender not recorded 0.9% ( $n = 2$ ). The mean age was 32 years (range 11 months – 94 years). The circumstances of the exposure were a) intentional (51.3%;  $n = 114$ ), b) accidental/therapeutic error (47%;  $n = 103$ ) and c) unknown intent (1.8%;  $n = 4$ ). Of the intentional overdoses, 83% ( $n = 95$ ) were symptomatic and required active treatment. The most common features reported were dizziness, ataxia, vomiting, blurred vision, tremor, tachycardia and decreased Glasgow Coma Scale (GCS). In all cases where the GCS was  $< 10$ , a mixture of drugs including alcohol were co-ingested. Carbamazepine was the only substance taken in 38.7% of cases ( $n = 86$ ), all of which had a GCS  $\geq 10$ . The majority of adult ( $> 12$  years) exposures ( $n = 192$ ) occurred in a domestic setting (74%;  $n = 142$ ); however 23.4% ( $n = 45$ ) of enquiries originated in a residential care home. Of these 93.3% of enquiries were due to accidental/therapeutic overdose. Only 6.8% of enquiries from residential settings were symptomatic with drowsiness and vomiting the most common symptoms. There were 30 enquiries (13.5%) concerning children (age  $\leq 12$  years) with a preponderance of boys (53.3%;  $n = 16$ ). All incidents occurred in a domestic setting. Only 16.7% ( $n = 5$ ) developed symptoms with vomiting ( $n = 3$ ), unsteady gait ( $n = 2$ ) and drowsiness ( $n = 1$ ); 46.6% ( $n = 14$ ) of children had no symptoms and 36.7% ( $n = 11$ ) had no recorded symptoms. **Conclusion:** Over 50% of cases involving carbamazepine were intentional overdoses and the majority (83%) of these were symptomatic. The GCS only fell below 10 when carbamazepine was ingested with other drugs and/or alcohol. A significant percentage, 93.3% of residential care home enquiries were due to therapeutic errors but less likely to have symptoms. All paediatric cases occurred in the home indicating that storage of medicines may not be adequate.

## 224. Radiation incident preparedness of Dutch hospitals

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**Objective:** The 2011 Fukushima nuclear incident and increasing terrorist threat underscore the necessity for hospitals to prepare for casualties of incidents involving radioactive material and/or ionizing radiation. This is also recognised in International Atomic Energy Agency (IAEA) Safety Standard "Preparedness and Response for a Nuclear or Radiological Emergency" (No. GS-R-2) that provides requirements for "Managing the medical response". To determine compliance with paragraph 4.78 that requires arrangements for "initial medical treatment of contaminated or highly exposed individuals in local medical facilities", the Dutch Poisons Center (PC) assessed radiation incident preparedness of Dutch hospitals. **Methods:** An online survey on resources and knowledge concerning management of casualties of radiation incidents was sent to all Dutch hospitals with a 24/7 available emergency department. Additionally, nine hospitals were visited for an in-depth interview. **Results:** The response to the online survey was 67% (58/87 hospitals responded). Most hospitals indicated that they prepare for the care of casualties of radiological incidents (86%). In small hospitals (<500 beds) the percentage is 77% and larger/academic hospitals almost all take into account radiation incidents. About two thirds of responding small hospitals, three quarter of larger hospitals and all academic hospitals can decontaminate casualties contaminated with radioactive material. The decontamination capacity is 1–5 persons/hour for most hospitals (83%) with increase in capacity with hospital size (maximum of 30 persons/hour for two larger/academic hospitals). Most hospitals have indoor decontamination facilities (70%) and a minority have outdoor facilities (e.g. decontamination tents). Of hospitals without decontamination facilities 75% have not made arrangements with other hospitals about referral of contaminated patients. Around 70% of hospitals describe radiological incidents in an emergency response plan but most hospitals do not specifically perform exercises with radiation incidents. A majority of hospitals (81%) knows that the Dutch PC advises on patient management after radiation incidents. **Conclusion:** In general, there is compliance with the IAEA "initial medical treatment" requirement in Dutch hospitals. The main recommendation from this study is that hospitals that are not yet prepared, either create decontamination facilities or make arrangements for referral of contaminated victims to a hospital with facilities. Additionally, it is recommended that hospitals make regional arrangements in advance about distribution of larger groups of casualties if their own capacity is limited. Finally, it is important to include emergency response to radiation incidents in a disaster relief plan and perform exercises.

## 225. Trends in colchicine exposures reported to the Poisons Information Centre Erfurt

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Poisons Information Centre, Erfurt, Germany

**Objective:** The Poisons Information Centre Erfurt has observed gradually increasing numbers of exposures to *Colchicum autumnale* since 2005, particularly due to confusion with *Allium ursinum*, whereas the number of exposures to various colchicine containing drugs was relatively consistent. We evaluated the causes and risks of these cases. **Case series:** Between October 1994 and October 2015, a total of 210 exposures to colchicine were reported. Of these 139 cases were exposure to *Colchicum autumnale* (in 55 cases uncertain) and 71 cases of (certain) exposure to various

colchicine-containing drugs. Of all 155 definite exposures, 31 cases (20%) were suicide attempts, 80 cases (51.6%) were accidental ingestions (about half of those in children) and in 5 cases (3.2%) adverse events at therapeutic doses had occurred. Medication errors were observed in 38 cases (24.5%), in which prolonged application of a therapeutic dose often resulted in at least gastrointestinal symptoms, but no fatality. Case 1: A 71-year-old female developed prolonged gastrointestinal symptoms after ingestion of three "leaf tips" of *Colchicum autumnale* in a suicide attempt. She was in intensive care for 4 days and was subsequently transferred to a psychiatric ward. Case 2: A 58-year-old male ingested 3 mg of colchicine per day over a period of 3 weeks and then reported to hospital with abdominal pain, diarrhoea, mild thrombocytopenia and elevated liver enzymes. Observation in hospital was recommended, however the further course is unknown. Case 3: A 89-year-old male with chronic pain syndrome and depression due to rheumatoid arthritis developed severe symptoms (gastrointestinal bleeding, dyspnoea, hypertension, first-degree atrioventricular block, lactic acidosis) resulting in multiple organ failure and death within 24 hours following the ingestion of approximately 100 ml Colchysat<sup>®</sup> (= 50 mg colchicine) in a suicide attempt. **Conclusion:** Severity of adverse and toxic effects, respectively, seems to increase proportionally to the administered dose and duration of use. Ingestion of parts of *Colchicum autumnale* plants often leads to at least gastrointestinal symptoms, even after a minor quantity. With pharmaceuticals, even doses not exceeding the recommended daily dose can lead to severe symptoms if taken over a longer period of time. Ingestion of large amounts (drugs or plants) usually results in severe gastrointestinal symptoms, multiple organ failure and death within 24 to 72 hours after ingestion.

## 226. Paediatric toxicology emergency simulation training: beyond discussions on "one pill can kill"

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**Objective:** Acute life-threatening paediatric toxicological emergencies are rare in most parts of the developed world. Current methods of critical paediatric poisoning typically involve didactic lectures and interactive case-based discussions on "one pill can kill" toddler toxicology. However, to be effective in the management of critically poisoned children, multi-factorial considerations are involved and not just textbook knowledge. It is postulated that high fidelity simulation training would be useful to augment existing methods of critical paediatric toxicology learning. **Methods:** A 4-hour high fidelity, high technology simulation training session involving only paediatric critical poisoning was conducted. Each simulation session was followed by a group debrief discussing the management and summarising critical toxicological and resuscitation learning points. Pre- and post-simulation surveys were done to assess the participants' assessment of their learning experience. **Results:** In total 11 physicians (6 paediatric emergency physicians, 3 paediatric medicine residents and 2 emergency medicine residents) underwent the high fidelity simulation course, during which 80% of the participants correctly identified the likely causative toxicological agents on just the history and physical examination alone. Despite this knowledge, however, when managing the simulated patients, there were significant delays and suboptimal management as more than half of the participants had fixation errors and were caught up in advanced cardiac and trauma life support algorithms. It was also noted that there needed to be broader approaches to include more common

differentials such as sepsis during the sessions. The participants reflected that the high fidelity simulation was very useful in providing a link in the gap between clinical knowledge and bedside application. **Conclusion:** High fidelity simulation training was useful and could be used to augment current methods of paediatric critical toxicology education.

## 227. The correlation between TOXINZ enquiries or National Poisons Information Centre calls and emergency department (ED) presentations

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**Objective:** ED staff within New Zealand have increasingly utilised the Internet accessible poisons information database TOXINZ. Accompanying this there has been a corresponding decline in telephone enquiries to the National Poisons Information Centre (PIC) from these professionals. This change in media for accessing poisoning management advice has implications for type of data collected by a PIC and may impact toxicovigilance functions. In particular, it is not known whether Internet poisons enquiries can be used for toxicovigilance purposes. The objective of this study is to identify if there is a correlation between TOXINZ or PIC enquiries and the poisonings that present to an ED. **Methods:** The records of all patients presenting with poisoning to the Wellington Hospital ED over the six year period (2007 to 2012) were reviewed to identify the most common pharmaceutical groups involved. Data was also extracted over the same time for TOXINZ enquiries from this ED, and from PIC records for the Wellington region. Yearly data were analysed in MS Excel™ 2010 and comparisons assessed using the Pearson product-moment correlation coefficient. This research was approved by the University of Otago Human Ethics Committee. **Results:** The number of presentations or enquiries during the six year period for paracetamol was: ED 750; TOXINZ 590; and PIC 826. For the anti-psychoics: ED 376; TOXINZ 733; and PIC 323. The benzodiazepines: ED 371; TOXINZ 252; and PIC 262. The selective serotonin re-uptake inhibitors (SSRIs): ED 362; TOXINZ 765; and PIC 263. For tricyclic antidepressants (TCAs): ED 116; TOXINZ 212; and PIC 127. For opioids: ED 326; TOXINZ 430; and PIC 417. Correlation coefficients for paracetamol exposure presentations to the Wellington ED, and TOXINZ and PIC enquiries for this drug were -0.28 and 0.85 respectively; for the antipsychotic group, 0.13 and 0.33; for benzodiazepines, -0.58 and 0.81; the SSRIs, 0.35 and 0.13; the TCAs, 0.37 and 0.25; and the opioids, 0.11 and 0.52. **Conclusion:** While high correlations with ED presentations were found for PIC enquiries regarding paracetamol and benzodiazepines, there was wide variation over the range of compounds reviewed (from 0.13 to 0.85). The results for TOXINZ were even less encouraging, with coefficients ranging from -0.58 to 0.37. It can therefore be concluded that, certainly in New Zealand, enquiries to an Internet poisons database from an ED do not reflect presentations of overdose, and that calls to a PIC from the region serviced by an ED are also an unreliable surrogate for presentations.

## 228. Behind the scenes of snow globe toxicity

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**Objective:** To report on enquiries to the UK National Poisons Information Service (NPIS) regarding snow globes and to raise awareness of potential toxicity from ingestion of their contents. **Methods:** Records of enquiries received by the NPIS were interrogated retrospectively between the 2008 and 2014 for any reference to the terms snow globe or snow scene. **Results:** A total of 57 enquiries involving 50 cases were received during the specified period. All exposures were accidental as a result of the item breaking or leaking. Children under 5 years accounted for 47 of the 50 cases, 70% of these involved males. Forty-six percent of cases were received in December and January which is unsurprising as snow globes are commonly used as Christmas decorations. The remaining cases were spread throughout the year. Forty two (84%) patients were asymptomatic. Where skin contact was reported ( $n=7$ ), pruritus and an erythematous rash occurred in three cases. Following ingestion ( $n=47$ ) features included coughing and mouth ulcers. In two cases, both involving children ingesting less than 20 mL, abnormal anion (AG) and osmolar gaps (OG) were reported. Case 1: AG 23.6 mmol/L, OG 10.8 mmol/L at 20 hours post-ingestion. Case 2: AG 21.6 mmol/L, OG 27 mmol/L at 6 hours post-ingestion. In both cases no clinical symptoms were reported and no antidote treatment for toxic alcohol poisoning was given. Unfortunately, further blood gas analysis and toxic alcohol concentrations were not available for either patient. **Conclusion:** Snow globes have previously contained fine fragments of bone/porcelain in distilled water. More recently however, contents have changed to calcium carbonate in distilled water with added glycerol to slow the fall of the fragments. Manufacturers have also started adding ethylene glycol, reportedly up to 20% of the volume of water [1] to reduce the risk of freezing during transit or storage. At time of writing no serious cases of toxic alcohol poisoning have been identified in these data or in published literature, but the abnormal blood results in these children warrant greater consideration as to the risks of poisoning via ingestion, particularly in young children.

### Reference

- [1] Patterson C, Bell-Davis P, Rawls H, et al. Ethylene Glycol Content of Snow Globes. *Clin Toxicol (Phila)* 2007;45:635.

## 229. A weight loss product containing fluoxetine

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**Objective:** In 2014 the Dutch National Poisons Information Center (DPIC) received 90 enquiries regarding the use of stimulating sport and/or slimming supplements resulting in effects such as tachycardia, palpitations, restlessness, nausea and vomiting. Here we report 5 cases of a Turkish weight loss product "Irem Naturel" which is available online throughout Europe and used, particularly in the Turkish community. It is highly promoted via social media and claims to be a safe, healthy and fast way to lose weight. The label states only herbal ingredients: red chili pepper, guarana, tragant gum, *Citrus aurantium*, starch and green tea. Capsules from one case were obtained by the DPIC and analysed by the National Institute for Public Health and the Environment. **Case reports:** In 2014, a 22-year-old female reported nausea after ingestion of 3 capsules of Irem Naturel. In March 2015, a 29-year-old female experienced anxiety, agitation, dry mouth, mild hypertension (120/100 mmHg) and tachycardia (136 beats/min) one hour after taking 1 capsule of Irem Naturel. Capsules from this case were obtained and laboratory analysis showed 30 mg fluoxetine, a selective serotonin reuptake inhibitor. In June 2015, a 41-year-old female experienced severe vomiting 2 hours after ingestion of 1 capsule. She was hospitalized for one day because of persistent vomiting. Capsules were not available for laboratory analysis. Two cases were reported in October 2015: a 1-year-old girl who ingested half a capsule and remained asymptomatic, and an 18-year-old female who attempted suicide with 20 capsules. Reported symptoms 3 hours after ingestion were dizziness, nausea and angina pectoris. It is not known whether these patients used other (prescribed) medicines at the time of the reported symptoms, or whether they used Irem Naturel for the first time. **Conclusion:** A food supplement for weight loss, marketed as being of herbal origin, contained fluoxetine. A previous sample of Irem Naturel from 2014 showed sibutramine. It cannot be excluded that some of the symptoms the patients presented with, were caused by fluoxetine or sibutramine. Nausea, vomiting, palpitations, and tachycardia are well known side effects of both drugs. Once again, this is a signal that healthcare practitioners need to be aware of the potential risks of these products. Poisons centers continuously need to screen their reports on food supplements, particularly for multiple enquiries about the same product. Collaboration with laboratory facilities is crucial to determine the composition of the supplements.

### 230. Is a urine toxicology report useful at the emergency department for patients who are intoxicated with benzodiazepines?

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**Objective:** The majority of cases of intoxication seen at Emergency Department of Moises Broggi Hospital, Barcelona, Spain involve medications, and the most common drugs involved are benzodiazepines. This study analyses the economic and clinical repercussions of demanding a urine toxicology report for patients with benzodiazepine intoxication. **Methods:** Urine toxicology reports were analysed in patients who registered at the Emergency Department (ED) with benzodiazepine intoxication in the period January to December 2013. **Results:** In 2013, 635 patients with poisoning were seen at the ED and 38% (243 cases) of these were due to drugs (alone or in combination with other substances), and 156 cases of these (64%) were due to

intoxication with benzodiazepines. Urine toxicology determination was carried out for 52 (33%) of these 156 cases, although 61% of these patients took benzodiazepines as usual treatment. In 100% of these cases the urine was positive for benzodiazepines. In addition, samples were also positive for cocaine ( $n=6$ ), cannabis ( $n=5$ ), tricyclic antidepressants ( $n=5$ ), methamphetamine ( $n=1$ ) and methadone ( $n=1$ ). All results impacted the final diagnosis without verifying them. Flumazenil was administered in 42% of the cases, and 17% of the patients required no treatment. The tests cost the hospital €2996.70 over the one year period. **Conclusion:** Urine toxicology testing did not influence treatment or the evolution of these patients and are costly to perform. To record a patient's medical history diagnosis of substance use based on these urine tests could pose a problem, both scientifically and legally.

### 231. A case of methanol intoxication treated with continuous renal replacement therapy

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**Objective:** Methanol poisoning is a medical emergency where rapid elimination of the toxin and its metabolite is crucial for recovery. Although serum methanol concentrations are helpful to decide the timing of start and termination of extracorporeal treatment, methanol assays are not a standard laboratory test in Korea. Here, we report a case of methanol poisoning treated with continuous veno-venous hemodiafiltration (CVVHDF), in which clinical improvement was confirmed with serum methanol concentrations. **Case report:** A 46-year-old Korean woman was brought to the emergency department in an unconscious state after ingestion of 150 ml of methanol. She was drowsy with a Glasgow Coma Scale (GCS) of E2V4M5. Her blood pressure was 100/70 mmHg and heart rate was 77 beats/min. The blood urea nitrogen and serum creatinine concentrations were 9 mg/dL (reference 8–20 mg/dL) and 0.6 mmol/L (reference 0.6–1.2 mg/dL), respectively. Initial arterial blood gas analysis showed metabolic acidosis (pH 7.180, pCO<sub>2</sub> 33.0 mmHg, HCO<sub>3</sub><sup>-</sup> 13.0 mmol/L). The serum osmolal gap and anion gap were 249 mOsm/kgH<sub>2</sub>O and 21.7 mmol/L, respectively. Despite the increase of central venous pressure from 5 cmH<sub>2</sub>O to 8 cmH<sub>2</sub>O after loading 2L of normal saline, hypotension continued. She was admitted to the intensive care unit and treated with CVVHDF and intravenous vasopressors. Following CVVHDF for 12 hours, GCS increased to E3V4M5 and the acid-base status of the patient returned to normal ranges. In

**Table 1.** Laboratory findings in a patient with methanol poisoning treated with continuous veno-venous hemodiafiltration.

Parameters	Day 1	Day 2	Day 3	Day 4
pH	7.180	7.348	7.493	NA
Bicarbonate (mmol/L)	12.3	11.9	26.9	NA
Osmolal gap (mOsm/kgH <sub>2</sub> O)	249	NA	-6	-6
Anion gap (mEq/L)	21.7	20.1	7.1	NA
Serum methanol (mg/L)	6547	1470	391	94

addition, blood pressure increased to 120/80 mmHg. We measured blood and urine concentrations of methanol during CVHDF and were initially 6546.9 ppm (mg/L) and 5895.1 ppm (mg/L), respectively. Following CVHDF, the serum methanol concentration decreased to 94 ppm (mg/L). She was discharged without complications on the fifth day. **Conclusion:** Measurement of serum methanol is useful in the management of methanol intoxication.

## 232. Circulatory effects of energy drinks after exercise

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**Objective:** Energy drink (ED) consumption has been associated with serious cardiovascular events,[1–2] and although not recommended after exercise, is frequently consumed after training sessions. The objective of this study was to evaluate the circulatory effects of EDs on recovery immediately after exercise and to compare the effects with intake of caffeine alone at rest. **Methods:** Fifteen healthy volunteers participated in two sessions of exercise by spinning on bicycles for 45 minutes, immediately followed by two units of EDs (Red Bull Light, total caffeine 160 mg) or the corresponding volume of a sports drink (Powerade 18 kcal/100 mL). Two weeks later the participants ingested the alternative drink in a crossover manner. Heart rate and blood pressure (BP) were measured after training and after 30 and 60 minutes of rest. Heart rate variability (HRV) was measured in three individuals for 12 hours. In another trial ten healthy volunteers ingested 3 units of ED (Red Bull, total caffeine 240 mg, taurine 3000 mg) at rest or the corresponding amount of caffeine in tablets (250 mg). **Results:** Pulse rate increased during the training session, decreased thereafter and did not differ between the two groups at rest. BP increased more in subjects that ingested ED compared to the sports drink. Systolic BP was 10 mmHg higher after 60 minutes, mean arterial pressure was 4.3 mmHg higher after 30 minutes and 7.7 mmHg higher after 60 minutes. Heart rate increased more after intake of ED compared to caffeine alone but was not significantly different. Both caffeine and ED increased PQ interval on the electrocardiogram (ECG). Systolic BP increased more with ED compared to caffeine alone but was not significantly different. Nine out of ten reported adverse symptoms (headache, nausea, palpitations, tremor) after ED compared to none after caffeine alone. **Conclusion:** Two units of EDs after exercise did not affect heart rate recovery after exercise, but BP increased significantly (probably due to the combined effect of taurine and caffeine). The physiological impact of this BP increase is unclear but may indicate a possible negative health effect.

## References

- [1] Sanchis-Gomar F, Pareja-Galeano H, Cervellin G, et al. Energy drink overconsumption in adolescents: implications for arrhythmias and other cardiovascular events. *Can J Cardiol.* 2015;31:572–575.
- [2] O'Brien MC, McCoy TP, Rhodes SD, et al. Caffeinated cocktails: energy drink consumption, high-risk drinking, and alcohol-related consequences among college students. *Acad Emerg.* 2008;15:453–460.

## 233. A study of *Phlomis olivieri* cytotoxicity

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**Objective:** Over 50% of drugs in clinical trials for anticancer activity were isolated from natural sources or are related to naturally-occurring compounds including Vinca alkaloids, vinblastine and vincristine isolated from *Catharanthus roseus*,[1] and the lignan derivatives, etoposide and teniposide.[2] The pharmacological activities of some *Phlomis* species such as antidiabetic, immunosuppressive,[3] anticancer and antioxidant activities [4] have been investigated previously. In this study we evaluated cytotoxicity effect of *Phlomis olivieri*. **Methods:** The flowering aerial parts of *Phlomis olivieri* were collected from the Khansar district of Pakistan for evaluation of its *in vitro* cytotoxic activity on different cell lines. We examined the antiproliferation effect of total methanol extract and different fractions including petroleum ether, chloroform, ethyl acetate, methanol and aqueous against colon carcinoma (HT-29), colorectal adenocarcinoma (Caco-2), breast ductal carcinoma (T47D) and Swiss mouse embryo fibroblast (NIH 3T3) cell lines using MTT assay. **Results:** According to the half maximal inhibitory concentration (IC<sub>50</sub>), the chloroform fraction and total extract of *Phlomis olivieri* exhibited high cytotoxic activity on all cell lines except Caco-2 cells but it had moderate antiproliferative effect on this cell line. In addition, the petroleum ether fraction demonstrated moderate cytotoxic effect on HT-29 cells although it had a high antiproliferative effect on other cell lines. IC<sub>50</sub> values confirmed that the growth and proliferation of HT-29 and T47D cells were most affected by chloroform, petroleum ether and total extracts due to their nonpolar compounds. Higher cytotoxic activity of nonpolar fractions may be due to the high content of germacrene D in their essential oil.[5] **Conclusion:** The results emphasize the importance of isolation and characterization of active components as well as the investigation of specific cytotoxic pathways which may help to determine whether the fraction is valuable for antineoplastic effects.

## References

- [1] Levêque D, Jehl F. Molecular pharmacokinetics of *Catharanthus* (vinca) alkaloids. *J Clin Pharmacol.* 2007;47:579–588.
- [2] Choi HJ, Cho BC, Shin SJ, et al. Combination of topotecan and etoposide as a salvage treatment for patients with recurrent small cell lung cancer following irinotecan and platinum first-line chemotherapy. *Cancer Chemother Pharmacol.* 2008;61:309–313.
- [3] Limem-Ben Amor I, Boubaker J, Ben Sgaier M, et al. Phytochemistry and biological activities of *Phlomis* species. *J Ethnopharmacol* 2009;125:183–202.
- [4] Kamel MS, Mohamed KM, Hassanean HA, et al. Iridoid and megastigmane glycosides from *Phlomis aurea*. *Phytochemistry* 2000; 55:353–357.
- [5] Sarkhail P, Amin G, Shafiee A. Composition of the essential oil of *Phlomis olivieri* Benth from north of Iran. *Daru J Pharm Sci* 2006; 14:71–74.

## 234. Public awareness about the market launch of mercury energy-saving lamps in Germany: assessment of an overhyped case of alleged poisoning

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**Objective:** Energy-saving lamps (ESL) are compact fluorescent lamps (FL) containing small amounts of mercury (Hg). Invented in 1926, they were produced in billions worldwide. The reducing of greenhouse gas emissions resulted in a ban on incandescent light bulbs (EU Parliament, 2009) and for replacement, the FL principle was miniaturized. A rapid self-declared public opposition argued against the EU legislation based on an early precedent case in Germany is reported here. An alleged "specialist" made a telediagnostic assessment of the case. His findings were distributed by almost all media. **Case report:** An ESL broke when a switched-on floor lamp fell over. The father picked up the remnants and discarded them. The next night, the 9-month-old male infant developed an acute pseudocroup. His 5-year-old brother developed a non-itchy rash all over his body and, 4 days after the breakage, progressive hair loss, which 4 months later also affected his eyebrows and lashes. After 8 months, this boy developed morning tremor of his hands and diarrhoea. The children were repeatedly examined by paediatricians, specialists in dermatology/allergology/environmental medicine and at an university environmental health centre. Neither the analyses of body fluids, and other clinical materials nor the ambient air measurements revealed any elevated concentrations of mercury, thallium or lead. Based on all available documents, no causal relationship could be established between the non-itchy rash, the temporary alopecia areata totalis and the mercury exposure. At the time the ESL was broken, both parents and children had been suffering from heavy respiratory tract infections, which could sufficiently explain the symptoms and signs observed. Nevertheless, this "psychodynamic event" triggered a highly interesting campaign against ESL in 2010. It reached its absolute culmination in a documentary entitled "Bulb Fiction" shown in cinemas (Austria 2011, Germany 2012) and produced countless enquiries (about 1000/year) to German Poison Centres without a single relevant case. **Conclusion:** As a result of the exaggeration of the risks, the young patient and his family became extremely unsettled and frightened. Due to the public pressure even governments failed to rely on objective criteria in their perspective, although a well-respected university institute could provide the necessary elucidation and technically correct assessment. Today, the overhyped case of alleged poisoning from an ESL has completely fallen into oblivion among the media and the public. The lesson to learn is that Poison Centres, in particular, have sufficient knowledge to fight against incorrect media coverage and exaggeration of risks.

## 235. Chlorprothixene overdose: analysis of enquiries to the Danish Poison Information Center

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**Objective:** Chlorprothixene has been marketed since 1959. Nevertheless, data concerning overdose are sparse. The aim of this register-based study was to gain knowledge on trends in poisonings in relation to prescribing patterns with this antipsychotic. **Methods:** We assessed all enquiries to the Danish Poison Information Center (DPIC) concerning chlorprothixene from 2007 to October 2015. Additionally, we searched the Register of Medicinal Product Statistics [1] in order to determine chlorprothixene prescribing patterns within the same period. **Results:** We identified 2422 enquiries concerning chlorprothixene poisonings over the study period. Chlorprothixene accounted for 32% of all enquiries regarding poisonings with antipsychotics. The number of chlorprothixene poisonings per year showed a small decrease throughout the study period. In addition, the fraction of chlorprothixene enquiries out of all antipsychotics decreased from 45% in 2007 to 23% in 2015, mainly due to an increased frequency of enquiries regarding other antipsychotics. Chlorprothixene was the seventh most common cause of contact to the DPIC regarding any medication in the study period. Within the last year, chlorprothixene was the fifth most common medication poisoning ( $n=314$ ) among antipsychotics, only surpassed by quetiapine ( $n=642$ ). The number of defined daily doses (DDDs) of chlorprothixene sold decreased through the study period, from 1,249,000 in 2007 to 1,060,000 (3.9% of all antipsychotics) in 2013. In contrast, 6,414,000 DDDs of quetiapine (23.6% of all antipsychotics) were sold in 2013.[1] **Conclusion:** To our knowledge, this is the largest study investigating trends in enquiries to a poison center regarding chlorprothixene poisonings. We found that the trend in enquiries reflected prescribing patterns (i.e. chlorprothixene DDDs sold), both decreasing through the study period. Nonetheless, the frequency of enquiries to the DPIC concerning chlorprothixene was found to be greatly out of proportion compared to a newer generation antipsychotic. This discrepancy was consistent throughout the study period. The frequency of chlorprothixene enquiries to our poison center was also high compared to previous analyses of poison center data.[2] The disproportionately high frequency of chlorprothixene enquiries may be due to pharmacological features of chlorprothixene, or characteristics of this particular patient population associated with an increased risk of overdose. This needs to be further investigated.

### References

- [1] The Danish Ministry of Health and Prevention. Register of medicinal product statistics; [cited 2015 Nov 20]. Available at: www.medstat.dk/
- [2] Fuhrmann M, Hruby K, Lenz K, et al. [New aspects of chlorprothixen-poisoning.] [Article in German] Wien Klin Wochenschr. 1982;94:150–153.

## 236. A systematic review of clinical presentations of cyanide poisoning

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**Objective:** There are inconsistencies in the medical literature describing clinical findings associated with cyanide toxicity.

The aim of this systematic review was to identify isolated cyanide poison cases and to identify reported signs, symptoms and laboratory findings. **Methods:** We searched MEDLINE, Cochrane Reviews, and Web of Science case reports and series using a number of medical subject headings (MeSH) descriptors pertaining to cyanide, toxicity, and poisonings. Exclusion criteria included studies on plants, laboratory analyses, smoke inhalation poisonings, animals as well as non-English articles and those where data were not available. Data extracted included demographics, exposure characteristics (e.g. cyanide salt type, route, and co-ingestants), acute signs/symptoms (e.g. neurological, respiratory, cardiac), medical management and outcome, laboratory results (e.g. levels of lactic acidosis, anion gap, cyanide, and thiocyanate). **Results:** From the initial 2964 articles retrieved, 60 articles (48 case reports, 12 case series) met inclusion/exclusion criteria and resulted in 107 patients. Males (71%), suicide exposures (65.4%), and oral exposures were most frequently identified among cases. Cyanide salts commonly implicated included potassium cyanide (51%) or sodium cyanide (9%). Most patients were lethargic (74%), hypotensive (55%), or had respiratory failure (70%); other signs and symptoms included change in pupils (26%), vomiting (22%), cardiac arrest (21%), seizures (19%), cyanosis (12%), cherry red skin (8%), and had an odor present (11%). In total 26% of patients died despite receiving care at a healthcare facility. Mean laboratory findings included: lactic acidosis (19.5 mmol/L), elevated anion gap (27.8 mmol/L), metabolic acidosis (pH 7.18), and bicarbonate (13.2 mmol/L). Medical management included, but was not limited to, intubation (64%), vasopressors (42%), cyanide antidote kit (sodium thiosulfate injection, sodium nitrite injection, amyl nitrite inhalant) (18%), sodium thiosulfate (40%), and hydroxocobalamin (38%). **Conclusion:** Contrary to general reviews published on cyanide toxicity, cherry red skin and bitter almond odor were rarely reported among published cases. Clinically, neurological, respiratory and cardiovascular adverse effects were commonly documented. Consistent with other studies, metabolic acidosis with significant lactic acidosis were the laboratory values consistently associated with cyanide toxicity. Clinicians should not depend on a bitter almond odor or cherry red skin to consider the diagnosis of cyanide toxicity in the critically ill patient with a significant lactic acidosis.

### 237. Paracetamol-protein adducts following acute paracetamol overdose

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**Objective:** Paracetamol-protein adducts (APAP-CYS) are a specific biomarker of paracetamol exposure. We sought to characterise APAP-CYS concentrations in patients with large paracetamol overdoses and/or paracetamol-induced hepatotoxicity. **Methods:** The Australian Paracetamol Project is a multi-centre prospective observational study that recruits patients through calls to the Poisons Information Centre (PIC) and clinical toxicology units in New South Wales. Patients were recruited from September 2013 to January 2015. Inclusion criteria included age >14 years, acute ingestion of paracetamol of  $\geq 35$  g, paracetamol concentration >300 mg/L at any time, or an ALT/AST >500 IU/L. Serum samples

collected were analysed for APAP-CYS. Peak APAP-CYS concentrations (C<sub>max</sub>) and time to peak concentrations (T<sub>max</sub>) were calculated. T<sub>max</sub> was calculated only in patients with more than 3 samples. **Results:** In total 335 samples from 53 patients were analysed. The median age was 24 years (14–71 years), with median reported ingested dose of 48 g (10–150 g). Median time to intravenous acetylcysteine was 6.8 h (1.25–77 h) post-ingestion. Patient data were stratified by peak ALT values; 27 patients had an ALT <50 IU/L or unchanged from baseline, with a peak APAP-CYS of 0.58 nmol/mL (0.22–1.71 nmol/mL) at a median T<sub>max</sub> of 14.7 h ( $n=23$ , 1–24.5 h). In this group, four patients of the 27 had an APAP-CYS concentration >1.1 nmol/mL. Seven patients had an ALT between 50 and 1000 IU/L, and a median APAP-CYS C<sub>max</sub> of 1.01 nmol/mL (0.3–2.4 nmol/L), at a median T<sub>max</sub> of 24 h ( $n=7$ , 12–32 h). Two of the seven had an APAP-CYS concentration >1.1 nmol/mL. Hepatotoxicity occurred in 19 patients (ALT >1000 IU/L) with median APAP-CYS C<sub>max</sub> 6.6 nmol/mL (1.5–43 nmol/mL), and T<sub>max</sub> of 60 h ( $n=14$ , 40–80 h). C<sub>max</sub> and T<sub>max</sub> in these patients were significantly greater than those from patients with ALT <50 IU/L ( $p<0.0001$ ). In those with abnormal transaminases, peak AST and ALT correlated with peak APAP-CYS concentrations,  $r$  value of 0.94 and 0.90, respectively. No correlation was noted for APAP-CYS and peak INR ( $r=0.78$ ). **Conclusion:** Previous studies of APAP-CYS found a significant correlation between peak APAP-CYS concentrations and AST or ALT, but not with the INR.[1] This study confirms previous findings and demonstrates that T<sub>max</sub> and C<sub>max</sub> differ for APAP-CYS as a function of ALT elevation. Four of 27 patients without liver injury had a peak concentration >1.1 nmol/L, which has been suggested as the threshold for identifying those with hepatotoxicity. This elevation of APAP-CYS likely reflects the sensitivity of the high performance liquid chromatography (HPLC) assay for APAP-CYS, compared to ALT assays.

### Reference

- [1] James LP, Capparelli EV, Simpson PM, et al. Acetaminophen-associated hepatic injury: evaluation acetaminophen-protein adducts in children and adolescents with acetaminophen overdose. *Clin Pharmacol Ther.* 2008;84:684–690.

### 238. Analytical confirmation of the synthetic cannabinoid receptor agonists (SCRAs) present in a cohort of presentations with acute recreational drug toxicity to an Emergency Department (ED) in London, UK

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**Objective:** Synthetic cannabinoid receptor agonists (SCRAs) are the most common novel psychoactive substances (NPS) reported in Europe over the last decade (142 reported to the end of 2014), but there is limited data available on the acute toxicity associated with their use. This study aimed to determine how commonly SCRAs were detected in patients presenting to our Emergency Department (ED) with acute recreational drug toxicity. **Methods:** A prospective observational cohort study enrolling consecutive adult patients who presented to an inner-city ED in London (UK) from January to July 2015 with acute recreational drug toxicity. Residual plasma from a blood sample taken as part of routine clinical care (which would have been discarded), was analysed using high-resolution accurate mass-spectrometry with tandem liquid-chromatography (HRAM-LC-MS/MS). Acquired data were processed against an in-house database containing all SCRAs reported to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) Early Warning System. Concentrations reported are based on a single-point calculation against the internal marker JWH-018. Minimum clinical data was obtained from ED medical records. This study had local institutional review board (IRB) approval. **Results:** Of the 179 individual patient samples analysed, 18 (10%) were positive for SCRAs. Of these 18, seven contained 1 SCRA, eight contained 2 SCRAs and three contained 3 SCRAs. The most common SCRA detected was 5F-AKB-48 (13 samples, concentration 50–7600 pg/mL); followed by 5F-PB-22 (7 samples, 30–400 pg/mL), MDMB-CHMICA (7 samples, 80–8000 pg/mL), AB-CHMINACA (3 samples, 50–1800 pg/mL), CUMYL-5F-PINACA (1 sample, 800 pg/mL) and BB-22 (1 sample, 60 pg/mL). Only 9/18 (50%) patients in whom SCRA were detected had self-reported SCRA use. On presentation, five patients (36%) had tachycardia (heart rate >120 bpm), one (6%) had Glasgow Coma Scale (GCS) < 8 and one (6%) had hyperthermia (38 °C). There were no recorded cases of significant hypertension (systolic blood pressure 160 mmHg). The most common clinical features were seizures and agitation both in 4 (22%) individuals; less common were psychosis and chest pain both in one (6%). Fourteen (78%) were discharged from the ED, of the four admitted to hospital one was admitted to critical care. **Conclusion:** SCRAs were found in 10% of this patient cohort presenting to the ED with acute recreational drug/NPS toxicity, however only half of those in whom it was detected self-reported use. This suggests that use of SCRAs is more common than expected and may be contributing to significant acute toxicity within recreational drug toxicity presentations to the ED.

### 239. Hepatotoxicity of novel psychoactive substances structurally related to 3,4-methylenedioxymethamphetamine (MDMA) and methamphetamine

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**Objective:** In recent years, many novel psychoactive substances (NPS) with amphetamine-like properties have emerged on the illicit drug market but data on their toxicity is scarce. 3,4-methylenedioxymethamphetamine (MDMA, “ecstasy”) and methamphetamine have previously been associated with liver toxicity.[1,2] Therefore, the objective of this study was to compare *in vitro* the potential hepatotoxicity of NPS with structural similarity to MDMA and methamphetamine. **Methods:** We treated human hepatoma

HepG2 cells for 24 hours with the NPS mephedrone, methedrone, methylone, 3,4-methylenedioxypyrovalerone (MDPV), naphyrone, and 6-(2-aminopropyl)benzofuran (6-APB) as well as MDMA and methamphetamine. We measured cytotoxicity, adenosine triphosphate (ATP) content, superoxide and lactate concentrations, total glutathione (tGSH) content, and the mitochondrial membrane potential. Additionally, we measured cytotoxicity and ATP content in metabolically competent human hepatoma HepaRG cells, with and without induction of drug-metabolizing enzymes. **Results:** All compounds produced concentration-dependent cytotoxicity and decreases in ATP content in HepG2 cells, with the exception of methylone, which did not cause a significant decrease in ATP content. We observed increases in superoxide and lactate concentrations for all substances while we observed a concentration-dependent depletion of tGSH for all substances except mephedrone. Furthermore, only MDPV and naphyrone decreased the mitochondrial membrane potential. In HepaRG cells, naphyrone and 6-APB caused cytotoxicity and decreases in ATP content while MDPV only decreased ATP. Hepatic enzyme induction did not alter the hepatotoxicity of the compounds. **Conclusion:** Our investigations showed that some of the investigated NPS lead to mitochondrial dysfunction. Naphyrone and 6-APB were considerably more cytotoxic than MDMA and methamphetamine in both cell lines and users of those drugs may therefore be at risk of liver toxicity.

### References

- [1] Antolino-Lobo I, Meulenbelt J, van den Berg M, et al. A mechanistic insight into 3,4-methylenedioxymethamphetamine (“ecstasy”) mediated hepatotoxicity. *Vet Q.* 2011;31:193–205.
- [2] Dias da Silva D, Carmo H, Lynch A, et al. An insight into the hepatocellular death induced by amphetamines, individually and in combination: the involvement of necrosis and apoptosis. *Arch Toxicol.* 2013;87:2165–2185.

### 240. *In vitro* pharmacological profiles of classic psychedelics and novel synthetic hallucinogenic substances and their relevance for clinical toxicology

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**Objective:** The aim of this study was to investigate the serotonin receptor activation and the monoamine transporter interaction profiles of classic and novel hallucinogens *in vitro*. **Methods:** We assessed binding affinities to several human monoamine receptors and functional 5-hydroxytryptamine receptor 2A (5-HT<sub>2A</sub>) and 5-HT<sub>2B</sub> receptor activation as well as norepinephrine (NET), dopamine (DAT) and serotonin transporter (SERT) inhibition in human cells stably expressing the respective human targets.[1,2] **Results:** Classic (lysergic acid diethylamide [LSD]), N,N-dimethyltryptamine [DMT], psilocin, mescaline, 2Cs) and novel (NBOMes, 2C-B-FLY, diisopropyltryptamine [DiPT]) hallucinogens potently interacted with serotonin receptors, in particular with the 5-HT<sub>2A</sub> subtype. Stimulants with no hallucinogenic properties such as amphetamine showed no interaction with the 5-HT<sub>2A</sub> receptor, as expected. 25I-NBOMe, 25B-NBOMe and 25P-NBOMe bound more

strongly to this receptor than LSD ( $K_i$ : 0.004  $\mu\text{M}$ ). Most compounds were partial agonists at the 5-HT<sub>2A</sub> receptor, but DiPT and 2C-B-FLY were full agonists. Additionally, 2C drugs, NBOMes, and LSD bound to trace amine-associated receptor-1 [TAAR1<sub>rat</sub>] and most 2C drugs and NBOMes activated the serotonin 5-HT<sub>2B</sub> receptor. NBOMes and LSD also exhibited low micromolar affinity at the  $\alpha_1$ -receptor. LSD was the only substance interacting with dopamine (D<sub>1-3</sub>) receptors at submicromolar concentrations. The tryptamines psilocin, DMT, and DiPT additionally inhibited serotonin reuptake ( $\text{IC}_{50}$ : 3.9, 3.1, and 0.9  $\mu\text{M}$ , respectively). Mescaline showed the overall weakest activity. **Conclusion:** Both classic and novel hallucinogens share a common action at the 5-HT<sub>2A</sub> receptor with some novel compounds exhibiting higher affinity to this target than LSD. Thus hallucinogenic properties are expected together with possible additional cardiovascular and stimulant effects with LSD and NBOMes via interactions with adrenergic  $\alpha_1$ -receptors.

## References

- [1] Rickli A, Luethi D, Reinisch J, et al. Receptor interaction profiles of novel N-2-methoxybenzyl (NBOMe) derivatives of 2,5-dimethoxy-substituted phenethylamines (2C drugs). *Neuropharmacology*. 2015;99:546–553.
- [2] Simmler LD, Buser T, Donzelli M, et al. Pharmacological characterization of designer cathinones *in vitro*. *Br J Pharmacol*. 2013;168:458–470.

## 242. Life-threatening amlodipine intoxication: a comparison of two approaches to treatment

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**Objective:** Management of calcium channel blocker poisoning represents a critical issue since conventional treatments including supportive care, catecholamines, calcium salts and insulin may fail, requiring rescue therapies suggested to be life-saving such as lipid emulsion, veno-arterial extracorporeal membrane oxygenation (ECMO) and albumin dialysis (MARS). However, evidence remains limited. We report two severe cases and discuss the modifications in amlodipine pharmacokinetics attributed to different therapies to clarify their contribution to the outcome. **Case reports:** Two female patients (51 and 68-years-old) were admitted hypotensive and conscious 4 hours after massive ingestion of amlodipine (3.6 and 0.9 g; plasma peaks: 451 and 664 ng/mL [therapeutic range: 1–25]), presenting refractory to mixed shock treated with massive doses of vasopressors. ECMO, lipid emulsion and MARS were implemented promptly during the first 24 hours following the assessment of refractoriness (1st case) and only when terminal organ failure occurred (2nd case, days 8–14). The first patient survived while the second died on day 14. Amlodipine was quantified (using liquid chromatography coupled to tandem mass spectrometry) in the plasma and the different MARS compartments including efferent and afferent blood, before/after albumin and charcoal cartridges, and in plasma treated after lipid emulsion with the measurement of the total

and non-trapped fractions. Terminal half-lives were determined by non-compartmental analysis during and after MARS session using PKsolver. Population modeling using Monolix software was used to characterize the role of MARS. Amlodipine terminal half-lives (30.9 and 92.6 hours) and observed clearances (74.6 and 10.7 L/h) were not altered during MARS. A one-compartment model, linear absorption and elimination provided the best fits for amlodipine pharmacokinetics with similar estimated parameters obtained with the non-compartmental method. A population model supported negligible MARS clearance. For both patients, extraction ratios (0.006 and 0.05%) and clearance (0.047 [0.01% of the observed clearance] and 0.43 L/h [4%]) due to MARS were extremely low. We evaluated the total extracted amlodipine at 2.668 and 6.169 mg. Extraction was mainly performed by the activated charcoal cartridge (35%) while the role of the anion exchange resin and dialysate was negligible. Lipid emulsion allowed trapping of 0% (when administered at ECMO implementation) versus 30% of the amlodipine (when administered on day 14 of ECMO). **Conclusion:** In life-threatening amlodipine poisoning, a strategy based on prompt multi-organ support may be life-saving allowing the transient replacement of failing organs and thus liver metabolism and renal elimination of amlodipine. Direct amlodipine extraction by MARS and lipid emulsion were of little contribution.

## 243. An inadvertent intravenous injection of 0.5% chlorhexidine in 70% ethanol in a newborn

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**Objective:** We report a case of unintentional intravenous injection of disinfectant 0.5% chlorhexidine in 70% ethanol in a newborn.

**Case report:** A female preterm neonate, 31 weeks of gestational age (birth weight 1370 g, length 39 cm, head circumference 28.5 cm and Apgar scores of 9/8) needed noninvasive ventilation for five days due to mild respiratory distress. After placing an umbilical venous catheter on the first day of life (DOL), it was replaced with a peripherally inserted central catheter (PICC) on the 5th DOL. On the 9th DOL during regular perfusion of the catheter 2.5 ml of 0.5% chlorhexidine in 70% ethanol was inadvertently injected into the PICC. The patient rapidly became unresponsive and apnoeic (oxygen saturations dropped to 38%), heart frequency was 135/minute, blood pressure 90/50 mmHg and capillary refill time 3 seconds. She needed bag ventilation and supplementation with oxygen. The cause of the child's sudden deterioration was identified in a few seconds so all infusions were stopped, the blood was pulled back from the PICC line and the ethanol content in the extracted fluid was determined to be 12 mmol/L. Haematuria appeared 30 minutes after the event. The baby was intubated, artificially ventilated and an umbilical venous catheter was reinserted. The blood ethanol concentration two hours after the event was 25.0 mmol/L, pH 7.23, bicarbonate 12.7 mmol/L, base excess -3.5 mmol/L. She was treated with sodium bicarbonate and control values 5.5 hours after the event were: blood ethanol 12.0 mmol/L, pH 7.61, pCO<sub>2</sub> 3.4 kPa, bicarbonate 25.5 mmol/L, base excess 4.6 mmol/L. Sixteen hours after the



event no residual ethanol was detected in the blood. A drop in hemoglobin and hyperbilirubinaemia were observed 2 and 5.5 hours after the event and she received a blood transfusion; her urine normalized after a few hours and hemoglobin remain stable. She was extubated the day after the event and needed noninvasive ventilation for additional 2 days. An ultrasound of the head showed bilateral nonhomogeneous areas of increased echogenicity periventricularly and the electroencephalogram showed no abnormalities. Her neurological status at discharge was appropriate for gestational age. **Conclusion:** An inadvertent intravenous injection of 0.5% chlorhexidine in 70% ethanol in a newborn resulted in abrupt circulatory and respiratory instability and hemolysis presenting with hyperbilirubinaemia and haematuria.

## 244. Self-extubation of the poisoned patients admitted to the intensive care unit: a major issue with limited consequences

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**Objective:** Self-extubation is a complication with possible severe risks in the mechanically ventilated patient. Considered a marker of care quality, the rate of self-extubation seems to be higher in poisoned patients, however, this is based on scarce data. Our objective was to study the incidence and consequences of self-extubation in poisoned patients in comparison to the non-poisoned patients. **Methods:** A retrospective single-centre descriptive study including all the patients admitted from January 2014 to June 2015 who were intubated, mechanically ventilated and further extubated; patient classification according to the etiology of intensive care unit (ICU) admission (intoxicated versus not intoxicated) and circumstances of extubation (self- versus planned extubation); univariate comparisons using chi-squared and Mann-Whitney tests. **Results:** During 17 months, 416 patients (53 years [41–69], 58% male) were intubated, mechanically ventilated (duration 2 days [1–4]) then extubated in the intensive care unit (ICU). These patients were tobacco smokers (41%), ethanol drinkers (31%) and drug users (14%), chronically treated with at least one psychotropic drug (57%) or with presenting chronic respiratory insufficiency (13%). ICU admission was related to acute intoxication (53%; including psychotropic drugs (78%), cardiotoxicant (18%) and household product ingestion (4%)) or causes not related to intoxication (47%; acute respiratory failure 30%, coma 30%, shock 25%, cardiac arrest 15%). The patients received sedation (92%; midazolam 80%, sufentanyl 83% or propofol 39%), catecholamines for shock (36%) and developed ventilation-associated pneumonia (14%). Before extubation, sedation was interrupted (97%), patients performed T-tube test (75%) but presented significant agitation (25%). Re-intubation was mandatory (10%), even immediately (2%) and post-extubation non-invasive ventilation used (15%). Non-planned, either deliberate (92%) or accidental (8%) extubation was observed in 20% of the patients. Self-extubation occurred more frequently in the patients admitted for poisoning (21% versus 17%,  $p < 0.05$ ) but was not more significantly responsible for re-intubation or related complications. Self-extubated patients more frequently presented agitation before extubation ( $p = 0.005$ ) but less frequently performed T-tube tests ( $p = 0.0002$ ).

**Conclusion:** Although predictable when the patient remains agitated despite mechanical immobilization, self-extubation is frequent in poisoned patients admitted in the ICU but does not result in significantly increased rate of complications compared to non-poisoned patients. Preventive measures should be implemented to reduce the rate of self-extubation including extubation under moderate and adapted sedation.

## 245. Acute methanol poisoning: prevalence and predisposing factors of haemorrhagic and non-haemorrhagic brain lesions

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**Objective:** To study the prevalence and predisposing factors of brain lesions in survivors of acute methanol poisoning. **Methods:** Clinical, biochemical and toxicological data on 106 patients hospitalized with confirmed methanol poisoning were collected prospectively during the Czech mass poisoning outbreak in 2012. Of 83 survivors, 46 patients (55%) had follow up examinations including brain magnetic resonance imaging (MRI) performed 3–8 and 24–28 months after discharge from hospital. **Results:** Of 46 patients with a median age of 49 (interquartile range [IQR] 35–57) years, 24 (52%) patients had a total of 40 abnormal brain findings with haemorrhagic lesions detected in 15 (33%) and non-haemorrhagic lesions in 9 (19%) patients. The patients with haemorrhagic brain lesions were more acidaemic (lower arterial blood pH, higher base deficit) and had higher glycaemia and lactacidaemia on admission than those without haemorrhages (all  $p < 0.05$ ). The patients with haemorrhagic brain lesions were administered ethanol in 11/15 cases, fomepizole in 3/15 cases, and no antidote was administered in one case. In the patients without brain haemorrhages ( $n = 31$ ), ethanol was administered in 24, fomepizole in 6, and no antidote in one case. Overall 41% (13/32) of patients with and 14% (2/14) without systemic anticoagulation had haemorrhagic lesions ( $p = 0.080$ ). Bleeding complications during the treatment occurred in 4/15 (27%) patients, and 5/15 (33%) had conditions predisposing to haemorrhage in the group with haemorrhagic lesions. In 3 cases with a series of computerised tomography (CT) scans/MRIs performed during hospitalization, the necrotic lesions in the brain remained non-haemorrhagic during hospitalization and haemorrhagic lesions were detected on the follow up MRI examinations only. **Conclusion:** No association between brain haemorrhages and systemic anticoagulation during dialysis was found. Brain haemorrhages might occur in severely poisoned patients treated without systemic anticoagulation, whereas treatment with high doses of heparin might not lead to brain haemorrhages.

## 246. Antidotal use of intravenous lipid emulsion: 5 years' experience in an intensive care unit

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**Objective:** Intravenous lipid emulsion (ILE) may successfully resuscitate patients with cardiotoxicity. However, the indications for its use, as well as its efficacy, are not sufficiently defined. **Methods:** An observational clinical study on the effects of lipid (Intralipid 20%) given as an intravenous infusion to a total dose of 500–1000 mL. The main criteria for administration of ILE were cardiocirculatory failure caused by liposoluble chemicals (drugs or pesticides) and poor response to conventional treatment which included dopamine, glucagon, bicarbonate and calcium chloride. Effects on blood pressure (BP), electrocardiogram (ECG) and survival of patients were assessed. **Results:** There were 31 patients (aged 28–83 years) treated with ILE, which comprised approximately 1% of the total number of patients hospitalized in the intensive care unit due to poisoning during 5-year follow up. ILE was most frequently used in calcium channel blockers poisoning (15 patients). In 9 patients who had ingested verapamil, or a combination of verapamil and benzodiazepines or angiotensin converting enzyme (ACE) inhibitors (enalapril, cilazapril), ILE was effective in reversing hypotension and dysrhythmias. There were 5 cases of multi-drug poisoning including amlodipine. Lethal outcome occurred in a patient poisoned by a combination of amlodipine with cilazapril, metformin and gliclazide. Combination of nifedipine and metoprolol was fatal despite treatment including ILE and pace-maker administration. Beta-blockers, including propranolol, metoprolol and bisoprolol were among the ingested drugs in 7 cases. Metoprolol was also lethal in combination with gliclazide, mianserin and benzodiazepines. Administration of ILE rapidly improved conduction delay and increased BP in cases of propafenone (1 patient) and glyphosate herbicide (1 patient) toxicity. In two cases of organophosphate insecticide poisoning with cardiovascular collapse, only transient increase of BP was noted. The remaining cases involved psychoactive drugs. ILE was successful in the treatment of clomipramine, maprotiline, sertraline and risperidone overdoses, but failed to reverse cardiotoxicity in patients who ingested carbamazepine, lamotrigine or valproate. **Conclusion:** Although all our patients received multiple therapies, the improvement observed in most of them soon after administration ILE can be attributed to its beneficial effects. Our experience revealed that the most invariable result of ILE administration was an increase in BP. The most impressive effect was the fast reversal of wide complex tachycardia in 3 different cases (ingestion of propranolol, glyphosate and propafenone) which may suggest effectiveness of ILE in the treatment of sodium channel blockade. However, ILE was not effective in all cases in which it could be expected on the basis of the toxic agent's liposolubility.

## 247. High sugar + low potassium + lactic acidosis = caffeine intoxication

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**Objective:** Increasing availability of high potency caffeine products over the Internet means the clinician will likely encounter patients intoxicated by this substance. Timely diagnosis can guide treatment and lead to a favourable outcome. We present a case where the diagnosis was initially overlooked and highlight signs that should lead the clinician to suspect caffeine poisoning. **Case report:** A 36-year-old woman with a history of bipolar disorder and access to topiramate, non-steroidal anti-inflammatory drugs (NSAIDs) and a “diet-pill” bought over the Internet, was brought to a country hospital by her husband. He had found her in a state of tremulous agitation and she had collapsed while vomiting and hit her head on the floor. On presentation she was drowsy and uncommunicative. Her heart rate was 170 bpm and blood pressure 90/50 mmHg. Upon return from a head CT scan (normal), she lost consciousness after developing ventricular fibrillation (VF) which responded to defibrillation. She continued to have multiple short episodes of VF and was treated with defibrillation and two 300 mg doses of amiodarone. She was intubated and transported by helicopter to a tertiary hospital where she was sedated with midazolam, propofol and fentanyl due to agitation and was defibrillated for short bouts of VF five times during the first hour. Multiple blood samples had demonstrated her to be hypokalemic (lowest value 1.5 mmol/L), hyperglycaemic (15–20 mmol/L) with lactate acidosis (highest value 18 mmol/L). This constellation of laboratory findings led to the suspicion of caffeine intoxication and drew attention to her “diet-pill” which an Internet search revealed to be of high caffeine content. She was treated with continuous veno-venous hemofiltration (CVVHD) for 15 hours during which time she remained tachycardic but had no further arrhythmias. She subsequently confirmed that she had taken fistfuls of her “diet-pills” in a suicide attempt, denying other ingestions. Serum caffeine 36 hours after the ingestion (post-CVVHD) remained elevated at 210 µmol/L and a nuclear magnetic resonance spectroscopy of a “diet-pill” revealed a caffeine content of 295 mg. The capsule, with the brand name “RoxyLean”, also contained nicotinic acid 33 mg, yohimbine 4 mg and traces of thiamine. **Conclusion:** Our case illustrates the need to recognize the signs and symptoms of caffeine toxicity. Although ultimately favourable, the outcome was by no means inevitable and timely treatment with beta-blockers could have been beneficial. Sympathomimetic symptoms in conjunction with the triad of hyperglycaemia, hypokalaemia and lactic acidosis should alert the clinician to the diagnosis.

## 248. Late presenting-massive acetaminophen overdose treated with liver dialysis

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**Objective:** To describe the successful use of extracorporeal therapy for a critically ill-late presenting acetaminophen overdose. Extracorporeal therapy (ECT) for acetaminophen overdose is generally not recommended. However, there are multiple case series suggesting its usefulness in early presenting massive overdoses. The EXTRIP group has made recommendations for ECT when

acetaminophen concentrations exceed 800 mg/L or when a patient presents with altered mentation or lactic acidosis with an acetaminophen concentration greater than 500 mg/L.[1] Molecular Adsorbent Recirculating System (MARS), also known as liver dialysis uses albumen impregnated dialysate membrane to enhance removal of protein bound toxins. MARS has also been shown to improve clearance of bile salts, ammonia, creatinine and urea, which can be used to improve encephalopathy secondary to acute liver failure. MARS supports hepatic function until native liver function recovers or can be used as a bridge to liver transplantation.[2] **Case report:** A 36-year-old female presented to the emergency department (ED) approximately 72 hours after intentional ingestion of about 200 pills of 500 mg acetaminophen. The patient presented to the ED secondary to abdominal pain and bloody emesis, she was described as being lethargic on the initial evaluation. Laboratory analysis revealed severe acidosis with a pH of 6.9, which only rose to 7.0 after 3 liters of normal saline and a sodium bicarbonate infusion. The initial acetaminophen (APAP) level was 28 mcg/mL, with aspartate transaminase (AST) 23,356 IU/L and International Normalized Ratio (INR) 2.8. Intravenous N-acetylcysteine was initiated per protocol. Over the next 12 hours, APAP was poorly metabolized and the concentration was 14 mcg/mL with a peak AST of 28,254 IU/L. Despite meeting King's College Criteria for acidemia, the patient was deemed unfit for liver transplantation. On day 2 of hospitalization, MARS was started. She remained on MARS for the following 3 days. The patient was finally transferred out of the ICU on hospital day 7 with an AST of 87 IU/L and an INR of 1.5. The patient survived to discharge without sequelae. **Conclusion:** We report a case of a critically ill late-presenting acetaminophen overdose which was successfully treated with liver dialysis. We believe MARS may be beneficial in this special circumstance, but requires further study.

## References

- [1] Gosselin D, Juurlink DN, Kielstein JT, et al. Extracorporeal treatment for acetaminophen poisoning: recommendations from the EXTRIP workgroup. *Clin Toxicol (Phila)*. 2014;52:856–867.
- [2] Mitzner S. Extracorporeal liver support-albumin dialysis with molecular adsorbent recirculating system. *Ann Hepatol*. 2011;10:S21–S28.

## 249. Critical care: survival without sequelae following a massive sodium nitrite ingestion

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**Objective:** To describe successful therapy in a patient with severe sodium nitrite poisoning after intentional ingestion who recovered completely within 24 hours. Our patient's initial methemoglobin concentration equals the previously reported highest methemoglobin concentration at 91%, after ingestion of an insecticide. This patient received two bolus doses of methylene blue (2 mg/kg) and an infusion for 48 hours resulting in hemolysis; she required three pints of packed red blood cells and ventilator support for nine days.[1] There are two prior reported cases of intentional sodium nitrite ingestion. Neither patient survived. Reporting our case highlights the beneficial effect of early, aggressive management of sodium nitrite ingestion, which likely allowed for our

patient's complete recovery. **Case report:** A 29-year-old male ingested 20–22 g sodium nitrite after fasting in a suicide attempt. Approximately 5 minutes later, he called Emergency Response. Paramedics found him obtunded, but following room air ventilation he was able to describe events. He subsequently became more obtunded, seized, and was intubated in the field. Upon arrival to the Emergency Department, his heart rate was 106 beats/minute, blood pressure 113/57 mmHg, respiratory rate 18 breaths/minute, and oxygenation saturation 86%. Physical examination was remarkable for severe cyanosis. He immediately received 140 mg methylene blue (methylthioninium chloride, estimated 2 mg/kg) intravenously. Arterial laboratory studies drawn one minute after methylene blue administration included methemoglobin concentration 91%, lactic acid 11.5 mmol/L and pO<sub>2</sub> 109 mmHg. He received 50 g activated charcoal. Repeat methemoglobin concentration approximately one hour after methylene blue administration was 54%. He was given an additional 150 mg methylene blue one hour after the first dose. Repeat methemoglobin concentration 24 minutes later was 35%. Since his hemoglobin was 11.6 mg/dL, he was given 2 units of packed red blood cells to enhance oxygen carrying capacity. Subsequent methemoglobin concentration was 6% and it was undetectable approximately 24 hours post-ingestion. He was transferred to the psychiatry service on hospital day 2 neurologically intact and without sequelae. **Conclusion:** Severe methemoglobinemia from intentional sodium nitrite poisoning can be effectively resuscitated using an aggressive approach with decontamination, methylene blue, and blood transfusion.

## Reference

- [1] George T, Shaikh AI, Thomas L, et al. Severe methemoglobinemia due to insecticide poisoning. *Indian J Crit Care Med*. 2014;18:113–114.

## 250. Unusual and severe cardiac effects in *Amanita proxima* poisoning: a case report

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**Objective:** *Amanita proxima* is one species of mushroom which can induce a type of poisoning called the "Proximien Syndrome" that is mainly characterized by early digestive symptoms, mild hepatic cytolysis and renal impairment. Its effect on cardiac function has not been established. We present a case of patient who developed "Proximien Syndrome" and cardiogenic shock. **Case report:** A 28-year-old male was admitted to hospital with vomiting and diarrhea that had started the night before. Symptoms occurred nine hours after eating a lot of mushrooms; his parents had eaten the same meal but were asymptomatic. On admission to a Medical Ward his blood tests showed impaired renal and liver functions: creatinine 3 mg/dL, urea 90 mg/dL, AST 240 U/L and ALT 350 U/L. The PCC of Milan was consulted; and the toxicologist suggested a diagnosis of hepatorenal syndrome caused by the consumption of *Amanita proxima*. We sent a picture of the mushroom ingested to a mycologist who confirmed it was *Amanita proxima*, Dumèe. The patient's renal function

deteriorated (creatinine 7 mg/dL, urea 120 mg/dL) and he became oligoanuric, so he was transferred to our Intensive Care Unit. As advised by the toxicologist our basic treatment included gastric lavage and activated charcoal and high volume fluid resuscitation with crystalloids. The patient's blood tests began to normalize, when he developed clinical signs of acute respiratory distress syndrome and hypotension. We diagnosed severe heart failure by echocardiography (reduced ejection fraction with very low cardiac output). Dobutamine and nitroprusside infusion were administered and he underwent endotracheal intubation and mechanical ventilation. The hemodynamic problem persisted for three days, but by the fourth day there was slow recovery of myocardial parameters. Dobutamine and nitroprusside were gradually reduced and by the sixth day he was breathing spontaneously and normotensive with progressive recovery as measured by echocardiography. **Conclusion:** *Amanita proxima* contains allenic norleucine, the toxin responsible for the reversible kidney damage, characterized by interstitial tubular nephritis with acute tubular necrosis and renal failure. The occurrence and seriousness of symptoms appears to be variable and dependent on the amount ingested. The case reported here suggests that *Amanita proxima* has the potential to cause severe cardiac toxicity necessitating early and precise cardiac examination in the management of patients poisoned by these mushrooms.

## Reference

- [1] Saviuc P, Danel V. New syndromes in mushroom poisoning. *Toxicol Rev.* 2006;25:199–209.

## 251. Mushroom picking in Navarre: safer than we think?

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**Objective:** The tradition of collecting and eating mushrooms in Navarre results in a remarkable number of accidental poisonings that are treated in hospital. We describe the characteristics of these poisonings and their severity. **Methods:** A retrospective descriptive study of patients presenting to the emergency department with suspected gastrointestinal intolerance and intoxication by consumption of mushrooms between January 2003 and October 2015. Statistical analysis was done using SPSS. **Results:** In this period, 319 patients were treated for mushroom poisoning; 56% were male and 44% female. Poisoning occurred most commonly in the autumn months (80% in September, October and November), and were most prevalent in October. Poisoning events occurred throughout the week and were not associated with any particular day. More than one person was involved in 50% of cases. The most frequent symptoms were mild gastrointestinal signs (85%), with latency of onset of symptoms of less than 3 hours (55%) or more than 6 hours (20%).<sup>[1]</sup> Most patients required only symptomatic treatment. In 12 cases there was neurological involvement, 4 had renal signs and 6 liver toxicity.<sup>[2]</sup> Only 38 patients provided a sample for mycological identification, but in five of these, identification was not possible. Most patients (70%) were discharged from the emergency service and 30% were admitted, mostly to the Observation Unit for less than 24 hours. Only three were admitted to an Intensive Care Unit (ICU). Activated charcoal was given to 22 patients and in 15 cases

specific antidotes were used.<sup>[3]</sup> No patients received a liver transplantation and none died. In 25% of cases the final diagnosis was intolerance to mushrooms. **Conclusion:** This study provides an update of poisoning by mushrooms in Navarre in the last 12 years. Poisoning occurred equally in both sexes and was most common during the autumn season, producing mild gastrointestinal symptoms with a short incubation period, requiring symptomatic treatment only. Mycological identification was only available in 10% cases. There were no serious complications or death in this case series.

## References

- [1] Pinillos MA, Gómez J, Elizalde J, et al. [Poisoning by foodstuffs, plants and mushrooms.] [Article in Spanish] *An Sist Sanit Navar.* 2003;26:243–263.  
[2] Díaz JH. Evolving global epidemiology, syndromic classification, general management, and prevention of unknown mushroom poisonings. *Crit Care Med.* 2005;33:419–426.  
[3] Benítez Macías JF, García Gil D, Brun Romero FM, et al. [Acute mushrooms poisoning.] [Article in Spanish] *Rev Clín Esp.* 2009;209:542–549.

## 252. Snake bite in Navarre: a retrospective analysis of 45 cases

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**Objective:** Snake bite is a common and frequently devastating environmental and occupational disease, especially in rural areas. Bites from crotalids and other snakes can induce severe complications, such as neurotoxicity, coagulopathy and renal failure. This study presents the epidemiological and clinical characteristics of snake bite in Navarre, Spain. **Methods:** A retrospective review of all reports of patients admitted to our emergency department from March 2003 to September 2014. The data included circumstances, sex, age, month the bite occurred, body part bitten, treatment and evolution. **Results:** In this period 45 patients were admitted due to suspected *Vipera* bite.<sup>[1]</sup> The sex-ratio was 0.125 (5 females, 40 males) with median age 31–50 years (55.6%). The highest number of snake bites <sup>[2]</sup> occurred in the spring and summer, with maxima in May (22.2%), July (15.6%) and September (5.6%) and minima in February and December (0%). The majority of patients were bitten in the upper extremities (77.8%). All cases were accidental exposures and the severity of poisoning was usually minor. Most of the patients (60%) were discharged from the emergency department and 40% were admitted, mostly (31.1%) to the Observation Unit for less than 24 hours. No patients were admitted to an Intensive Care Unit. Treatment was given to 88.9% (antibiotics 75.6%, antitetanic vaccine 42.5%, antivenin 2.5%). Antivenin was administered in only one patient, without any adverse reaction. No deaths were reported. **Conclusion:** This study provides us an update of snake bite in Navarre in the last 11 years. In our series, we only observe local symptoms with pain, local oedema and after a delay of several hours oedema of the limb. We did not observe any signs of blood abnormalities or neurotoxicity. The results could be characterized as unexpected, because, despite large rural areas in Navarre, the total number of snake bites were considerably lower than expected.<sup>[3]</sup>

## References

- [1] García Piney E, Fonseca Aizpuru EM, Nuño Mateo FJ. Mordedura de víbora grado II [Grade II snake bites]. *Medicina Clínica*. 2005;125:240.
- [2] Gold BS, Dart RC, Barish RA. Bites of venomous snakes. *N Engl J Med*. 2002;347:347–356.
- [3] Erce R, Arraiza JM. Estudio sobre incidencia de emponzoñamiento por ofidios en la Comunidad Navarra [Study on the incidence of envenomation by snakes in the Navarra Community]. *Comunicación a las IV Jornadas de AP de Navarra, Pamplona*. November 1992.

## 253. Variables associated with intensive care unit (ICU) admission in acute poisonings

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**Objective:** To analyze the variables associated with ICU admission in acute poisonings in a third level hospital. **Methods:** A retrospective descriptive study of acute poisoning treated at a third level Spanish hospital which required admission to the ICU over a 17 year period, between 1996 and 2012. **Results:** Out of a total of 18,283 patients admitted for acute poisoning over the 17 year study period, including pediatric emergencies, 719 (3.9%) patients required ICU admission. Their mean age was 40.8 (SD ± 17.7) years and 489 (68%) were male. The means of transportation most commonly used was an ambulance (31%), with major incidence on the weekend (Sunday 17.9% and Saturday 16.1%). In total 37.1% of patients had previous psychiatric disease, and for 43.8% it was their first poisoning. Oral was the most common route of exposure with 393 cases (54.7%). In total 201 (28%) cases involved a suicide attempt followed by drug overdose with 197 (27.4%). The most frequent etiology involved was the association of several medicines or medicines and drugs of abuse. The most frequently involved agents ordered by frequency and taking into account if there were multiple drugs involved or a single agent were ethanol 23% (13.7% single agent), benzodiazepines 17.9% (2.36% single agent), tricyclic antidepressants 6.3% (0.5% single agent), cocaine 6.1% (0.85% single agent), opiates 5.3% (1.25% single agent), neuroleptics 4.2% (0.69% single agent), caustics 2.9% (2.5% single agent) and pesticides 2.9% (2.22% single agent). The main clinical symptoms were 35.2% arrived in coma, 9.7% were agitated, 5.9% had convulsions and 1.9% arrived in cardiac arrest. Overall 22 patients (3.05%) admitted into the ICU died. **Conclusion:** Acute poisonings admitted to the ICU were most frequently acute oral poisonings in males due to a suicide attempt, without previous psychiatric disease, who arrived to the emergency room on the weekend by ambulance. The most frequently involved agents were alcohol and cocaine among abuse drugs, benzodiazepines and tricyclic antidepressants among the pharmaceuticals, and caustics and pesticides among the other types of agents. Multiple agent overdose was common. If we focus on the single agent poisoning, the most common agents were ethanol, caustics, pesticides and benzodiazepines. Only one third of patients are admitted with impaired consciousness and despite the severity of the symptoms the mortality rate was low.

## 254. What can toxicologists learn from therapeutic studies about the treatment of acute and chronic methotrexate poisoning?

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**Objective:** This study aimed to review acute and chronic methotrexate (MTX) overdoses as well as therapeutic studies that provide pharmacokinetic or clinical data on MTX to gain a better understanding of its toxicities. **Methods:** A retrospective audit was performed for acute and chronic MTX poisoning through the New South Wales Poisons Information Centre (NSW PIC) from April 2004 to July 2015 to determine the clinical syndrome and toxicity of MTX. In addition, a literature search was performed on poisonings and high dose MTX use, bioavailability, drug interaction and treatment. **Results:** In the NSW PIC data, there were 42 cases of acute MTX poisoning, 15 paediatric and one intrathecal overdose. Of the 26 adult patients, median age and dose were 47 years (IQR 31–62; range 10–85) and 325 mg (IQR 85–500, range 40–1000), respectively. Median reported paediatric age and dose were 2 years (IQR 2–2; range 1–4) and 50 mg (IQR 10–100). Of the patients who had serum MTX concentrations measured, none were above the nomogram. No patients reported adverse sequelae. There were 21 chronic MTX poisonings. Median age was 62 years (IQR 52–77), with stomatitis/mucositis (30%) and neutropenia (30%) the most common symptoms. There were 66 papers included in the review. Pharmacokinetic data showed that bioavailability is greatly reduced as oral doses increase with a possible ceiling dose in acute ingestion. Oncology data suggested that patients treated with an intravenous dose <1 g/m<sup>2</sup> MTX do not generally require or need folinic acid rescue. There is no feasible acute oral overdose that is likely to provide >1 g/m<sup>2</sup> of MTX or lead to serum MTX concentrations above the oncology folinic acid treatment line. In contrast, daily administration of low dose MTX for as little as three days has caused significant morbidity. However, the serum MTX concentration did not correlate well with toxicity or mortality in these patients. Glucarpidase is indicated in intrathecal MTX poisoning that exceeds 10 times therapeutic dose. Intravenous glucarpidase is not justified in oral overdose. **Conclusion:** Accidental oral MTX paediatric ingestion is unlikely to ever cause toxicity. In acute deliberate MTX poisoning, there are no situations in which toxicity would be expected to occur, although clinical experience confirming that are generally limited to overdoses ≤500 mg. In chronic poisoning, neutropenia and stomatitis/mucositis are sensitive markers of MTX toxicities. Folinic acid and supportive care are recommended until recovery. There is no rationale to monitor MTX concentration in either acute or chronic poisoning.

## 255. Plasma paracetamol metabolites accurately predict hepatotoxicity and represent new clinical toxicokinetic biomarkers

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**Objective:** Paracetamol (acetaminophen) is the commonest cause of liver toxicity in the Western world. Paracetamol is predominantly metabolised by conjugation to form non-toxic sulphate and glucuronide conjugates. A fraction is oxidized by P450 enzymes to form N-acetyl-*p*-benzoquinone imine (NAPQI), which reacts with glutathione (GSH) to form mercapturic acid and cysteine conjugates. When NAPQI production exceeds the capacity of GSH for detoxification it can bind to cellular proteins resulting in hepatocyte death. Our primary objective was to explore the toxicokinetics of circulating paracetamol metabolites in patients with and without acute liver injury (ALI) from the SNAP trial.[1] The secondary objective was to explore why more SNAP trial patients treated with the antiemetic drug ondansetron developed ALI. **Methods:** Paracetamol, paracetamol-glucuronide, paracetamol-sulphate (Para-Sul), paracetamol-GSH (P450 mediated), paracetamol-mercapturate (P450 mediated) and paracetamol-cysteine (Para-Cys) (P450 mediated) were measured in plasma from 116 patients before ("pre-treatment"), after 12 hours, and at the end of acetylcysteine (NAC) treatment for a single acute paracetamol overdose. Metabolite analysis was performed by liquid chromatography tandem mass spectrometry (LC-MS). **Results:** Patients who developed ALI had longer paracetamol half-lives and higher relative amounts of metabolites formed by P450. There was no difference between ondansetron and placebo or between NAC regimens. At pre-treatment the fraction of metabolites formed by the P450 pathway was significantly higher in patients that developed ALI (ALI 2.2% [1.0–3.6] versus no ALI 1.0% [0.6–1.6]  $p=0.0004$ ). Receiver operator curve (ROC) analysis demonstrated that the most accurate predictor of ALI was the ratio of Para-Cys/Para-Sul, with a ROC curve AUC of 0.91 (0.83–0.98). The current standard markers, alanine transaminase (ALT) and paracetamol had ROC-AUC of only 0.67 (0.50–0.84) and 0.50 (0.33–0.67), respectively. Post hoc analysis of the SNAP trial by logistic regression modelling demonstrated that when pre-treatment Para-Cys/Para-Sul was added to the stratified randomisation process the incidence of ALI in the ondansetron arm was not different from placebo. **Conclusion:** Paracetamol metabolites are toxicokinetic biomarkers that accurately stratify patients at presentation to hospital. They are superior predictors of toxicity compared with measurement of paracetamol parent drug and may refine patient care by identifying patients at risk of hepatotoxicity before current biomarkers are elevated. In the SNAP trial, by chance, more patients with a toxic metabolite profile at randomisation received ondansetron compared with placebo.

## Reference

- [1] Bateman DN, Dear JW, Thanacoody HK, et al. Reduction of adverse effects from intravenous acetylcysteine treatment for paracetamol poisoning: a randomised controlled trial. *Lancet*. 2014;383:697–704.

## 256. Digoxin-Fab antibody use in suspected chronic digoxin toxicity in elderly patients with multiple co-morbidities: does it make a difference?

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**Objective:** Bradycardia is common in chronic digoxin poisoning and often used as an indication to administer digoxin-Fab,

however 60% of patients treated with digoxin-Fab failed to increase heart rate more than 10 beats/min (bpm) 4 hours post-administration despite undetectable free serum digoxin concentrations.[1] **Methods:** Retrospective analysis of patients with suspected chronic digoxin intoxication; those treated with digoxin-Fab were compared to patients where it was not recommended (by the on-call toxicologist). Data included demographics, cardiac medications, presenting complaint, serum digoxin, creatinine and potassium concentration, digoxin-Fab dose, heart rate (HR) before and at various time points post-treatment with digoxin-Fab or post-consult time if not administered. **Results:** From August 2013 to October 2015, there were 47 consults: 21 digoxin-Fab recommended and 26 Fab not recommended. Mean age was 80.1 (48% female) versus 79.2 years (61% female), respectively. Digoxin-Fab was recommended more frequently when HR was <50 bpm and/or serum potassium >5 mmol/L with renal impairment. Patients receiving digoxin-Fab more frequently also took beta- or calcium channel blockers (CCBs) (95% versus 61%; OR 13.1, 95% CI 1.5–113) or potassium-increasing medications (95% versus 54%; OR 17.1, 95% CI 2.0–147), had elevated serum creatinine (76% versus 42%; OR 8.2, 95% CI 1.9–34), higher serum potassium (median 5.1 mmol/L versus 4.2 mmol/L,  $p=0.02$ ), higher serum digoxin concentrations (median 3.5 nmol/L versus 2.3 nmol/L,  $p=0.02$ ), and had pre-treatment HR ≤50 bpm (66% versus 31%; OR 4.5, 95% CI 1.3–15). Mean pre-treatment systolic blood pressure was Fab 129 mmHg versus no FAB 128 mmHg. Median Fab dose was 80 mg (range 40–160 mg). For patients with HR ≤50 bpm, mean HR before treatment was similar for both groups (Fab 37 bpm versus no FAB 39 bpm) and mean HR 4 hours (Fab 48 bpm versus no Fab 49 bpm) and 8 hours (Fab 55 bpm versus no FAB 54 bpm) post-treatment. For patients with HR >50 bpm, there was no change in median HR over time in either group. Seven patients died (5 Fab, 2 no Fab). **Conclusion:** Digoxin-Fab may be ineffective in treating bradyarrhythmias in elderly patients with elevated digoxin concentrations and multiple co-morbidities.[1] Increase in HR over time was similar in bradycardic patients irrespective of Fab treatment. Causes of bradycardia were multifactorial, including underlying cardiac disease, concomitant beta-blocker and/or CCB and/or potassium sparing drug use.

## Reference

- [1] Chan BS, O'Leary M, Isbister G, et al. The use of digoxin-specific antibodies in chronic digoxin poisoning. *Clin Toxicol (Phila)*. 2015;53:241.

## 257. Sri Lankan Russell's viper envenoming causes mild myotoxicity

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**Objective:** Russell's viper bites are reported to cause myotoxicity, but this is based on limited reports and is not routinely investigated for by clinicians. We aimed to investigate the incidence and severity of myotoxicity in Russell's viper (*Daboia russelii*) envenoming in Sri Lanka. **Methods:** Patients were prospectively recruited from the Teaching Hospital, Anuradhapura, in Northern Sri Lanka over a 13 month period from August 2013 to October 2014.

Information was recorded about bite circumstances, clinical presentation and laboratory investigations. Blood samples were collected and stored frozen for subsequent analysis for venom and creatine kinase (CK) concentrations. Only confirmed Russell's viper bite cases were included based on expert identification of the snake or later enzyme immunoassay to measure Russell's viper venom concentrations. CK was measured in patient samples using the Thermo Scientific Ltd CK-NAC reagent kit by adding reagent to serum samples and reading assays on a microplate reader. An abnormal CK was defined as  $>300$  IU/L. **Results:** There were 73 patients with confirmed Russell's viper bite with serum samples available for analysis. The median age was 40 years (13–65 years); 51 were male (70%). All 73 patients had local bite site effects. Evidence of systemic envenoming was present in 51 of the patients with coagulopathy ( $n=45$ ), myalgia ( $n=33$ ) and neurotoxicity ( $n=31$ ). Of the 33 patients that had myalgia, nine had generalised myalgia and 24 had localised myalgia only. Fifteen patients (21%) had a CK  $>300$  IU/L, 24 hours post-admission. Eight of these patients had serial serum samples available for analysis. Median peak CK in these patients was 842 (666–1065 IU/L). Of the 15 patients with CK  $>300$  IU/L nine had local myalgia only, three had generalised myalgia, one patient had no symptoms and information about symptoms was not available for two patients. Clinical evidence of myoglobinuria occurred in four patients; oliguria ( $n=3$ ), anuria ( $n=1$ ), loin pain ( $n=1$ ) and dark coloured urine ( $n=1$ ), but none of these patients had biochemical evidence of a high CK. Antivenom was given to 47 patients, one patient died as a result of a severe antivenom reaction. **Conclusion:** Russell's viper envenoming can cause myotoxicity but it is mild with peak CK concentrations of approximately 1000 IU/L and occurs in only one fifth of patients. Clinical evidence of myotoxicity did not correlate well with biochemical evidence, although local myalgia may simply represent local cytotoxic effects of the venom.

## 258. The use and safety of high-dose insulin euglycaemia therapy in toxin-induced cardiac toxicity

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**Objective:** Since its first reported clinical use in 1999, high-dose insulin euglycaemia (HIE) has been recommended in the management of toxin-induced cardiac toxicity. Its safety in low dose (0.5–2 U/kg/h) has been previously reported,<sup>[1]</sup> but higher doses up to 10 U/kg/h are now commonly recommended.<sup>[2]</sup> We report the use and safety of HIE in patients with toxin-induced cardiotoxicity. **Methods:** Cases were identified from the databases of two clinical toxicology units. Demographics, toxin(s) ingested, toxicity (minimum systolic blood pressure [SBP], use of inotropes and ventilation), insulin and glucose doses and duration, blood sugar concentrations, serum electrolytes (potassium, magnesium and phosphate), electrolyte replacement and outcome were extracted. **Results:** There were 13 patients (9 females), median age 56 years (15–88 years) treated with HIE over a 12 year period. There were 10 beta-blocker (metoprolol [5], propranolol [4], atenolol [1]) and two calcium channel blocker (verapamil and amlodipine) ingestions. One patient had funnel-web spider envenomation. Twelve patients had a SBP  $<80$  mmHg, 10 required inotropes in addition to HIE and six were ventilated. Insulin was commenced at a median time of 3.5 hours after admission (0.75–12 hours). Median loading dose in 12/13 patients who received a loading dose was 75 U (30–100 U) and the median maximum maintenance dose was 200 U/h (30–1500 U) with a median duration of 15 hours

(3–44 hours). Eleven patients developed hypoglycaemia ( $<3.5$  mmol/L) during insulin however seven patients developed hypoglycaemia after insulin therapy had been stopped. All patients received glucose infusions and this was continued for a median of 18 hours (3–34 hours) after ceasing insulin. Twelve patients developed hypokalaemia ( $<3.5$  mmol/L) despite replacement and one patient developed rebound hyperkalaemia ( $>5.0$  mmol/L) after insulin was stopped. Eight patients developed hypomagnesaemia (median 0.58 mmol/L [0.24–0.78 mmol/L]) and seven patients developed hypophosphataemia (median 0.47 mmol/L [0.21–0.99 mmol/L]). There were two deaths. **Conclusion:** Despite the beneficial effect of HIE in the management of toxin-induced cardiac toxicity, it causes significant disruption to glucose and electrolyte homeostasis. Large doses of glucose required during HIE appear to stimulate endogenous insulin secretion resulting in prolonged hypoglycaemia after cessation of HIE.

## References

- [1] Greene SL, Gawarammana I, Wood DM, et al. Relative safety of hyperinsulinaemia/euglycaemia therapy in the management of calcium channel blocker overdose: a prospective observational study. *Intensive Care Med.* 2007;33:2019–2024.
- [2] Engebretsen KM, Kaczmarek KM, Morgan J, et al. High-dose insulin therapy in beta-blocker and calcium channel-blocker poisoning. *Clin Toxicol (Phila).* 2011;49:277–283.

## 259. Extracorporeal life support (ECLS) in life-threatening digoxin overdose: a bridge to antidote

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**Objective:** Digoxin poisoning is potentially life-threatening and may result in refractory atrioventricular block and ventricular arrhythmias. Specific Fab fragments are very expensive and digoxin poisoning is very rare, therefore the likelihood of occurrence of a severe digoxin overdose in a setting where specific Fab fragments are not available is very high. Extracorporeal life support may allow time to obtain Fab fragments and serve as a bridge to antidotal therapy. **Case report:** A previously healthy 50-year-old male presented after ingestion of 22.5 mg of digoxin. Shortly after ingestion he experienced atrioventricular block followed by refractory electromechanical dissociation. The installation of arteriovenous extracorporeal support (provided by a centrifugal pump) prevented further development of multi-organ failure in this patient in refractory cardiac arrest while allowing time for Fab fragments to be obtained, as well as the infusion of that expensive antidote over a period of time, resulting in the optimization of the Fab fragments' binding capacity. The patient was in refractory electromechanical dissociation with a countable heart rate but without any difference between the systolic and diastolic blood pressures. An equimolar dose of digoxin-specific Fab fragment was administered as this results in the greatest amount of Fab eliminated in the urine bound to digoxin.<sup>[1]</sup> At the end of the Fab infusion the hemodynamic status normalized and the patient recovered fully. **Conclusion:** Digoxin-specific Fab fragments should be considered as first-line treatment for digoxin poisoning, however, in cases of sudden hemodynamic compromise, when Fab fragments are not immediately available, extracorporeal life support may be life-saving, and provide a "bridge to antidote".

## Reference

- [1] Schaumann W, Kaufmann B, Neubert P, Smolarz A. Kinetics of the Fab fragments of digoxin antibodies and of bound digoxin in patients with severe digoxin intoxication. *Eur J Clin Pharmacol.* 1986;30:527–533.

## 260. Intensive Care Unit admission in poisoned patients: a 14-year study

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**Objective:** The correct management of some poisoned patients may require admission to the Intensive Care Unit (ICU). We studied ICU usage in poisoned patients and the related features. **Methods:** A 14-year (1 July 2001 to 30 June 2015) prospective study including all patients admitted to our adult ICU with a main diagnosis of acute poisoning. We defined three criteria for ICU admission: the presence of vital function impairment (group 1), the perception that significant organ dysfunction could appear in asymptomatic patients on the basis of toxicokinetics or toxicodynamics (group 2), a clinical judgment for intensive observation in mildly symptomatic patients (group 3). **Results:** Poisoned patients admitted to ICU over the study period totalled 147 (2.8% of admitted patients) and 55.8% involved miscellaneous agents. All toxic agents were confirmed by toxicological laboratory analysis. The number of patients in each group was 115 for group 1, 12 for group 2 and 20 for the third. The average length of ICU stay (in days) was 3.87, 2.08 and 1.4 ( $p < 0.01$  compared to group 1 with Wilcoxon test), respectively. Ten patients died; three after paraquat ingestion, four due to a delay between poisoning and resuscitation (two 85-year-old patients with neurodepressant brain injury, one patient for heroin overdose and one for ethylene glycol), one for aspiration pneumonia as a consequence of an organophosphate ingestion, one for metoprolol ingestion and one due to hydrochloric acid ingestion. For group 1 the poisons were mainly benzodiazepines; these were detected at toxic concentrations in 47 patients. The main causes for impairment of vital functions were respiratory failure requiring ventilatory support (86.1%), severe cardiovascular toxicity (5.2%) and neurological dysfunction with a Glasgow Coma Scale  $< 11$  (8.7%). Group 2 toxins were paracetamol ( $n = 3$ ), acetonitrile ( $n = 2$ ), digoxin ( $n = 2$ ), ethylene glycol ( $n = 2$ ), paraquat ( $n = 2$ ) and metoprolol ( $n = 1$ ); the cases involving paraquat and metoprolol were fatal. All patients in group 3 had a good recovery and only one required ventilatory support owing to aspiration pneumonia. **Conclusion:** A rational approach to ICU use is described. Many poisonings (78.2%) presented an immediate life-threatening nature, while for patients who were asymptomatic or minimally symptomatic at admission, a short ICU stay was chosen for observation and treatment due to an unpredictable clinical course.

## 261. Rapid triage of victims of suspected chemical attack using a one-page questionnaire for identification of the toxidrome: the experience of Médecins Sans Frontières (MSF)

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**Objective:** In countries served by MSF, there is a high likelihood of chemical accidents and use of chemical weapons. The major issue is rapid identification of exposure to chemicals on a clinical basis in order to: (1) advise protection of rescuers and care givers at the scene, (2) provide adapted treatment to casualties, and (3) address the need for antidote supply. **Methods:** After reviewing the literature in major textbooks on acute chemical accidents resulting in a large number of casualties to identify easily collected clinical signs and symptoms, we composed a one-page questionnaire. There are presently three versions of the sheet, in French, English, and Arabic. Owing to the political context and analytical difficulties, we never attempted to precisely determine the agent having caused signs and symptoms but rather sought to identify the possible class of chemical involved and the toxidrome. **Results:** The one-page questionnaire was used in 6 settings: (1) a chemical incident following the opening of a chemical plan in Lubumbashi, Democratic Republic of Congo, in 2011, (2) the repeated use of anticholinesterase agents during the Syrian civil war from April 2013 up to the attack launched on the 21 August 2013, (3) repeated chlorine incidents in Syria since March 2014, (4) an attack using a vesicant agent towards civilians in August 2015 in Syria, (5) an outbreak of facio-truncular dystonic syndrome in North-East Congo, and (6) the acute onset of paraplegia in Mali in Summer 2015. In each setting, the analysis of the quoted items on the sheet made it possible to suggest a class of the toxicant involved within a few hours of exposure. In the case of exposure to chlorine and to the vesicant agent, two collections of signs over a period of a few hours were needed to draw a definitive conclusion. The lowest number of casualties in an exposure was three after exposure to vesicant agents. Early identification make it possible to advise adapted protection of care-givers at the site, advise attending physicians facing casualties at the time of presentation, and to define the need for antidote supply. **Conclusion:** The simple questionnaire listing relevant signs and symptoms made it possible to refine the toxidrome, including airborne pollution, attacks using anticholinesterase agents and chlorine and a counterfeit drug containing haloperidol. Repeated collection of signs may be required in agents acting progressively. A close collaboration with skilled toxicologists is needed when facing incidents involving hazardous materials.



## 262. Aerotoxic syndrome: aircraft involved in contaminated cockpit/cabin air exposure and related symptoms in 11 patients referred for review in a specialist clinical toxicology outpatient service

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**Objective:** Aircraft pressurisation typically occurs by using "bleed air" from aircraft engines. Contamination of bleed air and subsequently aircraft cabin/cockpit air by volatile hydrocarbons, organophosphates and/or other chemicals from the aircraft engine and/or engine lubricants is reported to cause a condition known as "aerotoxic syndrome". There is limited published clinical data in this area, with most information coming from "lay media" and other similar information sources. We describe our experience of patients referred to a clinical toxicology service for suspected "aerotoxic syndrome". **Case series:** We undertook a retrospective review of patients who had been referred to our UK specialist outpatient clinical toxicology service for suspected "aerotoxic syndrome". Data was extracted from the medical records on (i) occupation in relation to flying; (ii) aircraft suspected to be involved; (iii) details of single and prolonged contaminated air events; (iv) symptoms experienced; and (v) examination findings. We identified 11 patients (8 male, 3 female) with a mean  $\pm$ SD age of  $45 \pm 8$  years. Exposure was reported to be whilst working as a pilot (9 patients), cabin crew (1) and flying passenger (1). There was a wide range of aircraft types and configurations involved: Private business jets: 3 patients; Regional turbo-props (BAe ATP): 1 patient; Regional jets (Avro Jet/BAe146): 2 patients; Narrow-body single-aisle aircraft: Boeing 737/757: 3 patients and Airbus A319/320/321: 4 patients; Wide-body twin-aisle aircraft: Boeing 747/767/777: 4 patients; Airbus A330/340: 1 patient. Six reported  $\geq 1$  single "contaminated air event" whilst flying, of which 3 were subsequently confirmed on engineering review as being related to a failed oil seal; eight reported prolonged "exposure" to contaminated air (range of exposure 3 months to 8 years). The most common self-reported symptom was fatigue/lethargy (8 patients); other symptoms included: concentration/memory problems: 7; dizziness/light-headedness: 6; nausea/vomiting: 5; neurological symptoms (imbalance/numbness): 4; shortness of breath/cough: 3; irritability: 3; insomnia: 2; flu-like symptoms: 2; palpitations: 2; headache: 1. All patients had a normal neurological, respiratory and cardiovascular examination. Neurological imaging (magnetic resonance imaging and/or computerised tomography scan) was undertaken in 4 patients; all of which were normal. **Conclusion:** In this case series of 11 referred for review of potential "aerotoxic syndrome", there was no consistency in the aircraft involved and the range of symptoms reported was non-specific and not consistent with exposure to one specific toxin. Further large cohort studies are needed to fully understand and determine whether this is a true toxicological condition.

## 263. A characterization of occupational irritant and asphyxiant gas exposures

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**Objective:** Occupational exposures to irritant and asphyxiant hazardous gases are common. Some gases are known to result in morbidity and mortality, therefore characterizing these unintentional exposures may direct efforts for workplace controls. Therefore, the purpose of this study is to characterize occupational irritant and asphyxiant gas exposures. **Methods:** Retrospective cohort analysis of unintentional occupational exposures to irritant and asphyxiant gases reported to the National Poison Data System (NPDS) for the period from 1 January 2000 to 31 October 2014. **Results:** A total of 20,357 calls for unintentional occupational exposure to irritant and asphyxiant gases were reported to the NPDS during the study period. Carbon monoxide ( $n = 6457$ , 31.7%), chlorine ( $n = 4338$ , 21.3%), and simple asphyxiants ( $n = 2393$ , 11.8%) were the most common exposures. Most exposed employees were 20–29 years old ( $n = 6236$ , 30.6%) and male ( $n = 14,177$ , 69.6%). Inhalation or nasal ( $n = 17,994$ , 82.9%) and dermal ( $n = 1640$ , 7.6%) routes of exposure occurred most frequently. Reports of headache ( $n = 6997$ , 14.5%), nausea (4982, 10.3%), and dizziness/vertigo ( $n = 4641$ , 9.6%) were most common. Of those reporting specific contributing factors, most resulted from poor ventilation ( $n = 747$ , 36.4%) or generation of a toxic vapor or fume from mixing products ( $n = 489$ , 23.8%). Of the exposures, 11,965 (58.8%) were evaluated at a healthcare facility while 4923 (24.2%) were managed on-site. The majority of exposed cases were treated, evaluated, and released from care ( $n = 11,888$ , 58.4%) while others were admitted to a noncritical care unit ( $n = 1055$ , 5.2%) or required critical care ( $n = 656$ , 3.2%). Fresh air ( $n = 11,064$ , 33.1%) and oxygen administration ( $n = 7365$ , 22.0%) were the most frequent therapeutic interventions. Health outcomes ranged from no effect ( $n = 1416$ , 7.0%) to death ( $n = 61$ , 0.3%), but the majority suffered only a minor effect ( $n = 12,401$ , 60.9%). **Conclusion:** These data demonstrate that employees would benefit from additional workplace controls to prevent hazardous gas inhalational exposures and the aerotoxic syndrome. Proper mixing of chemicals and increased workplace ventilation are areas for training and design improvement. While most exposures resulted in mild effects manageable with minimal intervention, serious health effects can occur, including death. Given the potential for morbidity and mortality, identifying and mitigating workplace hazardous gas exposures should remain a priority for occupational and environmental medicine professionals.

## 264. Ethanol strips for bedside monitoring of ethanol concentrations during treatment of toxic alcohols: preliminary results

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**Objective:** Globally, ethanol is the most commonly used antidote in toxic alcohol poisoning. The typically recommended serum concentration is approximately 22 mmol/L (100 mg/dL). Due to the large inter- and intra-individual variation in ethanol metabolism, measurement of serum concentration is recommended every 1–2 hours.[1] In well-equipped hospitals, internal logistics and laboratory routines introduce a lag of at least one hour between sampling and reporting of the results. Where resources are limited ethanol assays may not be available at all. We therefore wanted to develop an easy-to-use, standalone bedside test based on dry chemistry. The first pre-prototype results are herewith presented. **Methods:** The testing principle is enzymatic, with a secondary indicator system giving a colour reaction to be assessed visually or by a dedicated reader. The system was designed for whole blood with a built-in blood separation system. Blood was applied to one side of the system, and readings were made on the opposite side. **Results:** From the visual readout, we found a concentration-dependent and visually distinct increase in the colour intensity. The first readouts on the meter showed a promising consistent curve with a linear correlation of  $R^2=0.9948$ . **Conclusion:** There is no viable simple ethanol test for bedside use currently available. The breathalyser requires an awake and cooperating patient, the samples cannot be drawn the first 30 minutes after oral administration of ethanol, and most importantly they do not distinguish between ethanol and methanol. The first results from our ethanol strips look promising for detecting ethanol accurately in the range of 6.5–65 mmol/L (30–300 mg/dL). The clinical usefulness in the presence of high methanol concentrations has not yet been fully assessed.

## Reference

- [1] McMartin KE, Jacobsen D, Hovda KE. Antidotes for poisoning by alcohols that form toxic metabolites. *Br J Clin Pharmacol.* 2016;81:505–515

## 265. Routine toxicological analysis does not meet clinical needs: An endless breakdown in spite of modern technology

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**Objective:** Diagnosis in clinical toxicology is based on clinical, biochemical, and analytical findings. The aim of this study was to assess the benefit of modern toxicological analysis in terms of confirmation of supposed ingested drugs (SID) reported by clinical toxicologists in daily practice. **Methods:** Cases of acute poisonings admitted to our Intensive Care Unit from 1 January 2014 to April 2015 were examined. Blood and/or urine specimens were collected on admission and sent to three different ToxLabs including (i) the local hospital (ToxLab A), (ii) for substances not assessed in ToxLab A, to ToxLab B which operates 24 hour a day; (iii) finally, for substances not detected in ToxLab B we sent to ToxLab C, a forensic Toxlab, working only during business hours. The two latter laboratories have mass spectrometry facilities. The ToxLabs received clinical information on the SID. The results for each patient were collected from each laboratory. Samples were positive or negative for SID/Toxicological analysis (TA). One positive

detection/quantification of a SID was considered SID+, TA+; the absence of a SID with positive TA: SID–, TA+; a SID+ with negative TA was considered SID+, TA–. The severity of exposure was assessed for drugs and alcohol using the maximum daily recommended dose for drugs (a therapeutic index (TI) > 1 denoted an intoxication) and a blood alcohol concentration of 0.4 g/L (>0.4 g/L was considered toxic). **Results:** The study included 224 occurrences of 90 SID in 70 patients. A SID+, TA+ was recorded in only 33% of the 224 occurrences; The TI was >1 in only 45% of the detected drugs of the SID+, TA+ group. In the SID–, TA+ group, the TA added 15% of patients initially considered SID–. However, in 79% of the SID–, TA+, the TI was less than 1, suggesting the analysis detected prescribed or recreational drugs in the SID–, TA+ group. **Conclusion:** In spite of large facilities, the benefit of modern analytical toxicology for the clinical toxicologist was low. We can question the accuracy of the SID, however, SID remains the standard for selection of drug of interest in acute human poisonings. The question is open as to whether high-resolution mass spectrometry may increase the benefit of TA. Presently we suggest a closer collaboration between clinical toxicologists and analysts to refine the actual needs in defining a list of toxicants of interest, based on SID, providing a regular update of this list of toxicants.

## 266. The evidence for acute tolerance to human alcohol intoxication (the Mellanby effect): a systematic review

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**Objective:** To establish the evidence for acute tolerance to human alcohol intoxication (the Mellanby effect [1]), which has been proposed to diminish the effects of a given blood alcohol concentration (BAC) during the descending part of the BAC-time curve. **Methods:** Multiple databases were searched using text words “tolerance,” “ascending,” “descending” or “Mellanby” with Medline term “exp \*alcohol/” or “exp \*drinking behaviour/” or equivalent. Full text articles were retained for analysis if they dealt with acute (within dose) alcohol tolerance in human subjects and provided quantitative data on both the ascending and descending limbs of the BAC-time curve. **Results:** Of 384 unique articles identified and screened, 125 full text articles were assessed and 19 met criteria for analysis. Most studies were small, median 10 (range 4–28) subjects per group. Doses of alcohol and rates of administration differed. All effects are dependent on drinking history and the degree of intoxication. We distinguished eight major outcome domains (physiological effects, hand-eye co-ordination, perception, decision-making, mental arithmetic and reasoning tasks, verbal skills, memory, subjective alcohol effects), and these were assessed by at least 24 different methods.[2,3] Ratings at a given concentration (C) were better (closer to sobriety) at C<sub>down</sub> (descending) than at C<sub>up</sub> (ascending) for subjects’ mean time for maze and peg-board tasks, arithmetic ability, and abstraction. Subjectively, those studied felt less drunk, and were twice as willing to drive at C<sub>down</sub> as at C<sub>up</sub>. By contrast, cognitive tasks, error performance, inhibitory control, visual memory and performance in a simulated driving task were worse at C<sub>down</sub>.

All values  $p < 0.05$ . **Conclusion:** The Mellanby effect is most firmly established for subjective intoxication. Confidence in ability to drive increases while measured driving ability falls. Objective measures of impairment are likely to be more robust than a person's own account.

## References

- [1] Mellanby E. Alcohol: its absorption into and disappearance from blood under different conditions. Gt Brit Medical Research Council, Special Report Series 1919; No. 31.
- [2] Marcziński CA, Fillmore MT. Acute alcohol tolerance on subjective intoxication and simulated driving performance in binge drinkers. *Psychol Addict Behav.* 2009;23:238–247.
- [3] Weafer J, Fillmore MT. Acute tolerance to alcohol impairment of behavioral and cognitive mechanisms related to driving: drinking and driving on the descending limb. *Psychopharmacology (Berl)* 2012;220:697–706.

## 267. Occupational transdermal poisoning with synthetic cannabinoids

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**Objective:** Synthetic cannabinoids are dangerous and unpredictable because their metabolites can bind to cannabinoid receptors up to 100 times more tightly than delta 9-tetrahydrocannabinol (THC) itself. In the pure state, these substances are either powders or oils that can be sprayed on herbal mixtures and sold in metal-foil sachets under different brand names. Herbal mixtures containing synthetic cannabinoids are most often smoked, and rarely ingested as an herbal infusion. We report symptomatic transdermal exposure to spilled oil of synthetic cannabinoid during a customs check. **Case series:** In 2014, three customs inspectors at the national airport in Slovenia opened a package imported from Hong Kong and labelled as a food supplement. They were not wearing protective gloves. One of thirteen one-litre bottles was broken during transport and they touched an unknown viscous and very sticky spilled substance with their fingertips. Despite washing their hands with water, dry mouth, nausea, blurred vision, dizziness, balance disorder, weakness, numbness and palpitations began to develop half an hour after exposure. On arrival at the Emergency Department six hours later they were somnolent, lethargic and confused. They showed signs of mydriasis, blurred vision, ataxia, weakness, numbness, tachycardia and orthostatic hypotension. Laboratory tests were within normal limits. The patients were treated with 0.9% sodium chloride only. Two days later they were feeling much better and reported amnesia and slowed perception of time after exposure. Subsequent toxicology analysis by liquid chromatography-tandem mass spectrometry (LC-MS/MS) revealed indazole-3-carboxamide based synthetic cannabinoid with IUPAC name 1-pentyl-N-(2-phenylpropan-2-yl)-1H-indazole-3-carboxamide in their blood samples. It was also confirmed with nuclear magnetic resonance spectroscopy (NMR) in oil samples seized at the airport. The detected synthetic cannabinoid is known among users as CUMYL-PINACA or SGT-24. **Conclusion:** In these patients occupational transdermal exposure to synthetic cannabinoid oil resulted in serious cannabinoid syndrome lasting for two days. Transdermal permeation of synthetic cannabinoids has been already shown in human skin in

an *in vitro* study.[1] Accordingly, limited skin contact with oil-containing synthetic cannabinoids can result in systemic poisoning and prompt washing with detergent and profuse rinsing is required.

## Reference

- [1] Valiveti S, Kiptoo PK, Hammell DC, et al. Transdermal permeation of WIN 55,212-2 and CP 55,940 in human skin *in vitro*. *Int J Pharm.* 2004;278:173–180.

## 268. Carbon monoxide poisoning in wood pellet storerooms

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**Objective:** Carbon monoxide (CO) is the leading cause of mortality due to unintentional poisoning in Slovenia. The main sources of CO in unintentional exposures are gas water heaters, wood stoves and fireplaces. Surprisingly, life-threatening CO concentrations were reported in wood pellets storerooms without combustion of carbon-containing organic material.[1] In Slovenia wood pellet heating has increased due to its cost-effectiveness, since wood pellets are made from natural compressed waste wood. We report a lethal CO poisoning and first responder CO exposure in a wood pellet storeroom. **Case series:** Eight firemen arrived at a wood pellet storeroom and began cardiopulmonary resuscitation on a cardiac arrested victim inside the storeroom. Soon after, they began to have headache, nausea, dizziness and fatigue. They decided to check the room for any presence of gas and, surprisingly, they detected a high CO concentration in the pellet storeroom, although no combustion of carbon-containing organic material had been noted. They escorted everyone out of the building and symptomatic firemen were immediately placed on high flow non-rebreathe 100% oxygen mask. On arrival to the Emergency Department they all reported headache and fatigue. Their carboxyhaemoglobin concentrations ranged up to 10%. They were continued on high flow non-rebreather oxygen until their symptoms resolved and they had normal concentrations of carboxyhaemoglobin. The victim died and autopsy confirmed CO poisoning. **Conclusion:** CO can arise from wood pellets kept in storerooms due to degradation processes of wood at average temperature, mainly in freshly produced or recently filled pellets.[2,3] Accordingly, wood pellets may constitute an occupational and domestic health hazard. Wood pellet storerooms should be continuously ventilated and equipped with CO detectors. First responders have to be aware of CO danger in wood pellet storerooms and victims should be evacuated as soon as possible and treated with 100% oxygen.

## References

- [1] Gauthier S, Grass H, Lory M, et al. Lethal carbon monoxide poisoning in wood pellet storerooms - two cases and a review of the literature. *Ann Occup Hyg.* 2012;56:755–763.
- [2] Svedberg UR, Högberg HE, Högberg J, et al. Emission of hexanal and carbon monoxide from storage of wood pellets, a potential occupational and domestic health hazard. *Ann Occup Hyg.* 2004;48:339–349.

- [3] Kuang X, Shankar TJ, Sokhansanj S, et al. Effects of headspace and oxygen level on off-gas emissions from wood pellets in storage. *Ann Occup Hyg.* 2009;53:807–13.

## 269. Pesticide exposure among professional users

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**Objective:** Pesticides are professional products largely used by farmers and gardeners. The identification of risks and the modality of acute exposure may have various clinical manifestations, from irritating symptoms to severe cases of systemic functional and organ damage. We describe toxic professional acute exposures to pesticides. **Methods:** A 5 year (2010–2014) retrospective review of cases of professional acute exposures to pesticides and herbicides managed by the Pavia Poison Centre (PPC) was performed. Included cases were assessed for sex, age, agent involved, modality of exposure and PSS (Poisoning Severity Score) at first evaluation by a specialist toxicologist. Attempted suicides were excluded. **Results:** In total 439 cases were included (95% males; mean age  $52.5 \pm 16$  years). Concerning the agents involved, insecticides accounted for 42% of cases (245/439) and, among these, organophosphates and pyrethroids were more common (45% and 30% of cases, respectively). Herbicides (19%; 110/439) were often involved (19%), with glyphosate representing 57% of these cases. Other agents were fungicides (18%), copper and sulphur (11%) and miscellaneous other products in 4% of cases. In 6% of cases the agent involved was unknown. In general, only one product was involved in 74% of cases, 2 products simultaneously in 18%, 3 products in 6% and 4 products in 1% of cases. The exposure occurred during the use of the product in the 67% of cases, accidentally in 5% and during the preparation of the product in 3%. This information was unknown in the 26% of cases. Inhalation and dermal contact were the main routes of exposure (72% and 17% of cases, respectively). Concerning the PSS at first evaluation by the PPC, patients were asymptomatic in the 10% of cases, presented mild symptoms in 68%, moderate symptoms in 10% and serious symptoms in 1% (unknown in 10%). Mortality occurred in 0.1%. **Conclusion:** The main predisposing factor for exposure was inappropriate use of pesticides, associated with the incorrect use of personal protective equipment. In addition to playing a fundamental role in the diagnosis of intoxication, the PPC also provides specialized advice to evaluate correct indications for antidote administration and to supply antidote in an adequate amount. To reduce potential risk of intoxication, especially in occupational setting, a correct preventive information program may be essential.

## 270. Pneumomediastinum after intentional injection of MDPV and cannabinoids into the jugular vein

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**Objective:** Infectious complications after intravenous injection of synthetic cathinones ("bath salts") are considered to occur more often compared to intravenous misuse of other drugs. In addition, injection-related injuries may be more relevant than toxicity or infection.[1] We describe a case of severe local injury related to the intravenous administration of drugs with a favourable outcome. **Case report:** A 29-year-old woman was admitted with auditory and visual hallucinations after repeated self-injection of methylenedioxypropylvalerone (MDPV) and "Jamaican Gold Extreme" into the jugular vein and soft tissue of the neck over the course of several days. Her level of consciousness varied between somnolence and agitation with otherwise normal vital signs. She had an infraorbital haematoma and subcutaneous emphysema. Cerebral computerised tomography (CT) scan excluded signs of fracture or cranial bleeding. A small dorsobasal pneumothorax without rib fractures was seen on X-ray. A subsequent CT scan of the neck and thorax revealed excessive cutaneous air deposits from the base of the skull to the lower mediastinum, including a pneumopericardium. Laboratory analysis showed only minimally elevated inflammation parameters and normal myocardial markers. Electrocardiography was normal. Oesophageal injury was excluded via gastroscopy. Bronchoscopy was considered dispensable due to absent signs of perforation on the CT scan. After interdisciplinary discussion with our surgeons, we decided on a conservative treatment strategy, including calculated antibiotic therapy and intravenous fluids. The patient recovered over the next 5 days and was discharged. A follow up CT scan showed decreasing mediastinal, pericardial and cutaneous gas accumulation. Urine gas chromatography-mass spectrometry (GC-MS) analysis found traces of MDMB-CHMICA (a cannabinoid receptor-1 agonist) but cathinone exposure could not be verified due to the delay between exposure and admission. **Conclusion:** This case demonstrates that severe complications after injection of synthetic cathinones and cannabinoids may occur independent of systemic drug toxicity. Here, a presumably massive intravenous air deposition due to hallucinations and agitation during injection occurred. Despite the risk of bacterial mediastinitis or pericarditis and the hazard of air embolism, the patient recovered without surgical intervention. In the absence of signs of local or systemic infection and the lack of mechanical complications, judicious clinical observation with a conservative treatment strategy may promote a favourable outcome. To our knowledge, this is the first case describing these complications in a patient after intravenous "bath salts".

## Reference

- [1] Belton P, Sharngoe T, Maguire FM, et al. Cardiac infection and sepsis in 3 intravenous bath salts drug users. *Clin Infect Dis.* 2013;56:e102–e104.

## 271. Intoxications handled in the intensive care unit

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**Objective:** Acute intoxication is a frequent situation in the emergency department and some patients need to be handled in the Intensive Care Unit (ICU) due to the severity of poisoning. Our study examines the epidemiology of acute intoxication admitted to the ICU of our hospital. **Methods:** A descriptive and prospective study was carried out analysing all patients diagnosed with

intoxication admitted to the ICU, in a second level hospital, during a 5 year period. The statistical analysis was carried out with SPSS, to analyse the following variables: age, sex, psychiatric background, toxic agent, initial Glasgow Coma Scale (GCS), length of stay, treatment, psychiatric evaluation and mortality. **Results:** Only 32 cases were admitted in the ICU. These cases comprised 1.4% of the total poisoning patients that the hospital over the 5 year period ( $n = 2269$ ). The average age was 50 years old (58% women) and 81% of patients were Spanish. In total 69% of patients had a psychiatric background and 63% had suicidal premeditation. Most exposures occurred in the home (94%). The majority of cases involved drugs (69%); benzodiazepines represented 34% of cases and polypharmacy overdose was found in 71%. Alcohol was involved in 29% of cases with drugs or abuse drugs. The clinical signs reported included neurological (72%) and respiratory (28%). The average of GCS was 8. A third of patients (66%) required mechanical ventilation due to neurological depression. Antidotes were used in 59%, most commonly flumazenil (50%) and naloxone (31%). Activated charcoal was administered to 34% of patients. Renal replacement measures were carried out in only one case (valproate intoxication). Urine screening testing was requested in 53% of cases. The average length of stay was 5 days. Half the patients (50%) had psychiatric evaluation and a third (34%) were transferred to a psychiatric hospital on discharge, 22% to a mental health centre, 16% to an internal medicine unit and 13% were discharged home. Death occurred in 16%. **Conclusion:** Acute intoxication that requires admission to the ICU of our hospital represents a small percentage of total intoxications. The most common profile is a middle-aged woman with a background of psychiatric disorders, who takes multiple drugs (mostly commonly benzodiazepines), with suicidal premeditation, resulting in neurological manifestations requiring mechanical ventilation in a high percentage of cases. The high mortality correlates with the severity of poisoning in these patients.

## 272. Bitter almond ingestion causing life-threatening intoxication

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**Objective:** Life-threatening intoxications with bitter almond (*Prunus dulcis amara*) are rare and seldom described in the literature.[1–3] Bitter almond contains amygdalin which is hydrolyzed to cyanide in the intestine. The lethal dose of cyanide is considered to be 0.5–1 mg/kg. One gram of bitter almond may produce 2–2.9 mg of cyanide.[4] A case of profound lactic acidosis after bitter almond ingestion is presented. **Case report:** A 28-year-old woman complained of nausea and shortness of breath. On arrival at hospital she was deeply unconscious with a Glasgow Coma Scale (GCS) score of 4–5. She had a bradycardia of 40 and was severely hypotensive with an unrecordable blood pressure but weak carotid pulse. Naloxone and flumazenil were given without effect. Arterial blood gas showed a profound metabolic acidosis (pH 6.5, base deficit 30 mmol/L, lactate >20 mmol/L, PaO<sub>2</sub> 26.4 kPa and PaCO<sub>2</sub> 7.19 kPa). She was intubated and received intravenous crystalloid infusions and phenylephrine. When information was received that empty bags of bitter almonds (80 g in total) had been found in her room she was immediately given 5 g of intravenous hydroxocobalamin prior to referral to a tertiary care hospital and another 5 g during transportation. During the next 12 hours her lactate slowly decreased and her arterial blood gas finally normalized with a lactate of 1.8 mmol/L. In addition (as further absorption of cyanide from remaining almonds in the intestine could not be excluded) she

was given 15 g of intravenous sodium thiosulphate. The day after her GCS score was 15 and she was extubated without complications. **Conclusion:** Cyanide intoxication due to bitter almond ingestion is rare but may be the cause of inexplicable severe lactic acidosis. In addition to general supportive care hydroxocobalamin is an efficient antidote.

## References

- [1] Sanchez-Verlaan P, Geeraerts T, Buys S, et al. An unusual cause of severe lactic acidosis. Cyanide poisoning after bitter almond ingestion. *Intensive Care Med.* 2011;37:168–169.
- [2] Shragg TA, Albertson TE, Fisher CJ Jr. Cyanide poisoning after bitter almond ingestion. *West J Med.* 1982;136:65–69.
- [3] Nader R, Mathieu-Daudé JC, Devaux M, et al. Child cyanide poisoning after ingestion of bitter almonds. *Clin Toxicol (Phila).* 2010;48:574–575.
- [4] Toomey V, Nickum E, Flurer C. Cyanide and amygdalin as indicators of the presence of bitter almonds in imported raw almonds. *J Forensic Sci.* 2012;57:1313–1317.

## 273. Death following suicidal dinitrophenol ingestion can occur in France too

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**Objective:** Dinitrophenol is an uncoupling agent of phosphorylation used by bodybuilders as a fat-burner. Despite its use in humans being illegal in numerous countries, cases reports of fatalities with dinitrophenol overdoses are reported, especially in the UK and US.[1,2] The clinical picture of poisoning includes profuse sweating, tachycardia, tachypnoea, agitation, seizure, yellow discoloration of the skin, muscles rigidity and uncontrolled hyperthermia. In the most severe cases, patients die due to a cardiovascular collapse.[1,3] **Case report:** A 26-year-old healthy bodybuilder ingested 15 pills of dinitrophenol with suicidal intent. A few hours later, at the arrival in the emergency unit, the reported symptoms were agitation, vomiting, profuse sweating, hyperthermia of 40 °C, tachycardia of 170 beats/minute (bpm), and tachypnoea (50 breaths/minute). Alkalosis, hyperkalaemia (7.1 mmol/L) and hyperlactataemia (2.3 mmol/L) were the most important biological disturbances. Despite management in the intensive care unit (ICU), 20 minutes after arriving at the hospital, tachycardia worsened to 192 bpm, tachypnoea to 60 breaths/minute, his skin and urine were yellow, his muscles became profoundly rigid, and he required sedation and intubation. At least 5 minutes after he was intubated, a cardiac arrest occurred and muscle rigidity made mechanical ventilation very difficult. Adrenaline and cardiac massage were ineffective and the patient died 1 hour after admission to ICU. **Conclusion:** This first case in France of death after consumption of dinitrophenol in the context of a bodybuilder's suicide attempt is proof that this fat-burner, although not legal, is present in our country. The Internet allows ready access to such chemicals.

## References

- [1] Grundlingh J, Dargan PI, El-Zanfaly M, et al. 2,4-dinitrophenol (DNP): a weight loss agent with significant acute toxicity and risk of death. *J Med Toxicol.* 2011;7:205–212.
- [2] Kamour A, George N, Gwynnette D, et al. Increasing frequency of severe clinical toxicity after use of 2,4-dinitrophenol in the UK: a report from the National Poisons Information Service. *Emerg Med J.* 2015;32:383–386.
- [3] Bartlett J, Brunner M, Gough K. Deliberate poisoning with dinitrophenol (DNP): an unlicensed weight loss pill. *Emerg Med J.* 2010;27:159–160.

## 274. A case of mono-intoxication with duloxetine: clinical presentation and serum concentrations

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**Objective:** Even though duloxetine as a more recent serotonin-norepinephrine reuptake inhibitor is used increasingly in the therapy of depression or as a co-analgesic treatment, mono-intoxications along with serial blood concentrations have rarely been reported. We report such a case here following intentional overdose in an elderly patient. **Case report:** An 80-year-old female with a history of depression and attempted suicide was admitted 10 hours after ingestion of the contents from delayed release capsules of duloxetine (6–9 g). Approximately 1.5 hours after ingestion she vomited twice and developed dizziness, epigastric pain, and heartburn. On admission she was conscious and stable with no cardiorespiratory effects. Later she developed impairment of vision, tremor and disorientation. Her electrocardiogram (ECG) showed a prolonged QRS time (120 ms), which might have been pre-existing, but did not demonstrate a prolonged QTc interval. She was treated symptomatically and recovered fully. Five days after admission she was transferred to the psychiatry ward. Blood samples were taken at 10, 24, 30, 46, and 97 hours after ingestion. The duloxetine serum concentrations were 1830 ng/mL, 3350 ng/mL, 3000 ng/mL, 2490 ng/mL and 1490 ng/mL, respectively. Terminal half-life was markedly prolonged. **Conclusion:** Despite the rather high serum concentrations and dosage of duloxetine in our case report, severity of symptoms was unexpectedly mild. In contrast, coma has been associated with a serum level of 860 ng/mL [1] and death has been reported following a duloxetine overdose as low as 1 g. [2] Inter-individual susceptibility to the cardiotoxic properties of duloxetine or the absence of co-ingested drugs may be an explanation for the mild clinical signs exhibited by this patient. Further data are required to estimate whether duloxetine mono-intoxications, even with high doses, may be safely managed by observation only. In case of ingestion of delayed release-preparations of duloxetine, administration of activated charcoal may be reasonable even beyond one hour after ingestion, in light of the prolonged half-life of duloxetine observed in this case.

## References

- [1] Kruihof MK, Bruins NA, van Roon EN. Coma after overdose with duloxetine. *Ann Pharmacother.* 2011;45:e5.

- [2] Lilly USA. Cymbalta (Duloxetine Delayed-Release Capsules) for oral use. prescribing information; [cited 2015 Nov 26]. Available at: <http://pi.lilly.com/us/cymbalta-pi.pdf>

## 275. A case of severe envenoming by eastern diamondback rattlesnake

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**Objective:** Although bites by non-indigenous poisonous snakes have become fairly common in European countries, most cases still represent serious challenges for poison control specialists due to lack of experience in dealing with similar cases, non-availability of specific antisera or the combination thereof, as was the case with the patient reported here who was bitten in Trzic, Slovenia, approximately 50 km from Ljubljana. **Case report:** A 37-year-old professional snake handler was bitten on his hand by an adult female eastern diamondback rattlesnake (*Crotalus adamanteus*) while cleaning its terrarium cage without using proper protection. Upon admission, approximately one hour after the bite, he was alert, without signs of gastrointestinal, circulatory or respiratory distress. The bite wound consisted of a small laceration on the medial aspect of the proximal interphalangeal joint of the third finger and two bleeding fang marks on the interdigital fold between fingers 4 and 5. The swelling extended proximally just above the wrist. He had paresthesiae and intense local pain. The laboratory revealed signs of systemic coagulopathy with hypofibrinogenemia. As the case was initially ruled to be a mild envenomation he was given six vials of specific antiserum (Antivypmin<sup>®</sup>) but the swelling progressed rapidly. A large subcutaneous haematoma formed on affected limb, so the patient was given what remained of the available antiserum (an additional two vials). Some six hours after the bite he became obtunded and hypotensive. The edema worsened further, blisters formed and the pain became intolerable. An emergency fasciotomy was required due to signs of compartment syndrome before we could arrange for additional antiserum from the nearest available location. The antiserum was sent from Vienna General Hospital almost 400 km away and delivered to Ljubljana by plane. After he was given additional doses of antiserum, clinical progress was uneventful, except for mild rebound thrombocytopenia. The patient was transferred to the Department of Plastic Surgery and afterwards to a rehabilitation institute due to the need of further physical therapy. **Conclusion:** This serious envenomation by an eastern diamondback rattlesnake, which ultimately required a fasciotomy, illustrates the usual dilemmas which face poison control specialists in similar settings, in particular regarding the procurement of specific antisera.

## 276. Toxin induced myocardial stunning with improvement in cardiac contractility after intravenous lipid emulsion administration

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**Objective:** Myocardial stunning is defined as myocardial dysfunction following a brief episode of severe ischemia with gradual return of contractile activity. It has also been described following toxic overdose of many substances. Free fatty acid oxidation is impaired in the stunned myocardium and it has been shown to recover in tandem with improvement in contractility. Research in animals using intravenous lipid emulsion (IVLE) treatment has demonstrated an improvement in contractility in stunned myocardium after hypoxic injury.[1] **Case report:** A 25-year-old woman was found unresponsive and with signs of aspiration. She had a temperature of 35 °C, heart rate of 126 bpm, blood pressure of 76/55 mmHg, and oxygen saturation of 78%. She was cyanotic and had diffuse rhonchi on her pulmonary exam and 2 mg intranasal naloxone followed by 0.4 mg intraosseous naloxone were administered without significant effect and the patient was subsequently intubated for hypoxic respiratory failure and airway protection. In addition to the hypotension and hypoxia she had an episode of hypoglycemia shortly after arrival to the Emergency Department (ED). Despite aggressive fluid resuscitation with over 8 liters of isotonic saline, steroids, norepinephrine and broad-spectrum antibiotics, there was no significant improvement in hemodynamics as a bedside cardiac ultrasound demonstrated decreased left ventricular ejection fraction with global hypokinesis. Immediately following this a 100 mL bolus of 20% lipid emulsion was administered. Over the next 30 minutes the patient's blood pressure began to increase and the need for vasopressor support decreased over 50%. Repeat cardiac ultrasound showed improvements in rate and cardiac contractility. Within 24 hours the patient was weaned from pressors and extubated. She reported ingestion of clonazepam and heroin although her toxicology screen was also positive for trazodone, gabapentin, citalopram and nicotine. She was discharged, without apparent sequelae, 4 days after arrival. **Conclusion:** We report a case of a multidrug overdose with respiratory failure and subsequent myocardial stunning, for which administration of IVLE immediately improved cardiac contractility and hemodynamics. This case suggests that IVLE may be a useful adjunct to supportive care in cases of drug-induced myocardial stunning. Additional research is warranted.

### Reference

- [1] Van de Velde M, Wouters PF, Rolf N, et al. Long-chain triglycerides improve recovery from myocardial stunning in conscious dogs. *Cardiovascular Res.* 1996;32:1008–1015.

## 277. Severe methaemoglobinaemia and the blue infusion

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**Objective:** Sodium nitrite is an oxidizing agent that is used to preserve and cure meats, and is known to cause severe methaemoglobinaemia. We report a case of life-threatening methaemoglobinaemia after intentional sodium nitrite ingestion, requiring large doses of methylene blue. **Case report:** A 19-year-old, 75 kg male presented to hospital via ambulance, one hour after intentional ingestion of unknown quantity of sodium nitrite. On examination, he was drowsy, with oxygen saturation 88% on oxygen, heart rate (HR) 155 beats/min (sinus tachycardia) and blood pressure (BP) 115/60 mmHg. He was intubated on arrival and 90 minutes post-ingestion received a 100 mg intravenous bolus of methylene blue (methylthioninium chloride). Five minutes later he deteriorated with BP 75 mmHg [systolic] and oxygen saturation 63% (on 100% oxygen). Bloods taken after methylene blue showed methaemoglobin concentration 80.7% and lactate 6.5 mmol/L. He was resuscitated with 3 L of intravenous fluid, but remained hypotensive (89/50 mmHg). Two hours post-ingestion a further 50 mg methylene blue was administered, as this was all that could be located at the time; thereafter the methaemoglobin concentration remained unchanged (81%, lactate 7.6 mmol/L). Three hours post-ingestion he remained unstable (HR 140 beats/min, BP 100 mmHg (systolic) and lactate 8 mmol/L). A methaemoglobin concentration could not be obtained, due to laboratory difficulties with the high concentration. As he was unstable a further bolus of 150 mg methylene blue was given three hours post-ingestion. At five hours, the methaemoglobin concentration was 64% with HR 120 beats/min, BP 130 mmHg (systolic) and lateral ST depression and T wave inversion on an electrocardiogram (ECG). At this stage a methylene blue infusion was commenced at 1 mg/kg/h because of ongoing methaemoglobinaemia. He remained on this infusion for five hours until methaemoglobin concentrations were 30% and lactate 2 mmol/L. The infusion was then reduced to 0.5 mg/kg/h for a further four hours and discontinued once the methaemoglobin concentration was 10%. He was extubated a day later and was grossly neurologically intact. **Conclusion:** Cases of sodium nitrite ingestion causing methaemoglobinaemia have been reported in the literature with some patients requiring two, 2 mg/kg boluses of methylene blue.[1] This is a case of severe methaemoglobinaemia (80%), requiring repeated boluses and an infusion of methylene blue for ongoing methaemoglobinaemia.

### Reference

- [1] Sohn CH, Seo DW, Ryoo SM, et al. Life-threatening methemoglobinemia after unintentional ingestion of antifreeze admixtures containing sodium nitrite in the construction sites. *Clin Toxicol.* 2014;52:44–47.

## 278. Clinical and renal ultrasound aspects in vitamin D poisoning: a case of poisoning in twins

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**Objective:** To present the connection between clinical and renal ultrasound aspects in two cases of vitamin D poisoning. **Case report:** Twin sisters aged 2 years and 5 months presented in our clinic for anorexia, constipation and weight loss (3 kg in the last month). From their history we noted that 18 months previously they had both been diagnosed with rickets by their general

practitioner and received treatment with vitamin D3 and calcium. They had received a total dose of 4,600,000 IU of vitamin D3 intramuscularly (October  $10 \times 100,000$  IU, May  $10 \times 200,000$  IU, January  $8 \times 200,000$  IU). They had also received oral calcium for 10 days during these months. The symptoms started one month after discontinuation of the treatment. No pathological signs or symptoms were noted at physical exam. Biochemical tests revealed hypercalcemia (total calcium 15.6 mg/dL with ionized calcium 6.9 mg/dL and 16.3 mg/dL with 7.36 mg/dL [normal values total calcium 9–10 mg/dL and ionized calcium 4–5 mg/dL]), hypercalciuria (300 mg/24 h and 180 mg/24 h [normal values 4 mg/kg/24 h] and high serum 25-hydroxy vitamin D concentrations (240 ng/mL and 245 ng/mL [normal values 30–100 ng/mL]). Ultrasound examination revealed bilateral nephrocalcinosis in both patients. They both received a calcium restricted diet and corticotherapy (pulse therapy of methylprednisolone 10 mg/kg/day for 3 days and then oral methylprednisolone 1 mg/kg/day for 14 days). On day 15 they were in good condition, with good appetite, normal gut transit and normal values of calcium (total calcium 10 mg/dL with ionized calcium 4.7 mg/dL and 10.1 mg/dL with ionized calcium 4.8 mg/dL). Ultrasound examination still showed nephrocalcinosis. They were discharged in the 16th day and received a calcium restricted diet for 6 months and then a low calcium diet (250 mg/day) for another 12 months. Three months later 25-hydroxy vitamin D concentrations and calciuria normalized but ultrasound changes persisted. Nephrocalcinosis was no longer present on ultrasound after 12 months in one of the girls and 18 months in the other. **Conclusion:** In the initial stage of vitamin D poisoning there is a concordance between the presence of clinical, biochemical signs and renal ultrasound changes.[2] Clinical and biochemical changes disappeared 2 weeks after corticoid therapy [1] while ultrasound images of nephrocalcinosis resolved after 12–18 months.[2]

## References

- [1] Ginsburg B. Vitamins. In: Nelson LS, Levin NA, Howland MA, et al., eds. *Goldfrank's Toxicologic Emergencies*. 9th ed. New York, USA: Mc-Graw Hill Medical; 2011:609–623.
- [2] Ulmeanu C. Vitamin Poisoning. In: *Acute Poisoning in children and adolescents*. Tridona Oltenița 2015;219–220.

## 279. Pneumothorax – a severe event in acute hydrocarbons poisoning in children: a case report

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**Objective:** To present a rare and severe event that can occur in acute hydrocarbon poisoning in children. **Case report:** A 2-year-old girl was admitted 4 hours after ingestion of an unknown quantity of diesel fuel. On admission she had dyspnea (respiratory rate 60/minute), cough, tachycardia (heart rate 150/minute), vomiting and somnolence. Blood tests showed white blood cells (WBC)  $11,000/\text{mm}^3$ , platelets  $253,000/\text{mm}^3$  and hemoglobin 11.9 g/dL. Chest radiography revealed imprecisely delimited opacity in the right lower lobe and a few small areas of opacity in left lower lobe. She was started on ampicilin and sulbactam IV and a glucose and electrolyte infusion. Three hours later she suddenly became cyanotic and febrile, and her dyspnea and tachycardia worsened. Physical examination of the lung revealed the

absence of breath tone in the right lung. The second chest radiography showed massive right pneumothorax and multiple large areas of opacity with conjunction tendency in the left lung. Repeated blood tests revealed WBC  $24,000/\text{mm}^3$ , platelets  $478,000/\text{mm}^3$ , hemoglobin 10 g/dL and pH 7.28. She was transferred to the intensive care unit where pleural drainage was performed, oxygen was given and antibiotic therapy was reconsidered. Meropenem, vancomycin and fluconazole were introduced and methylprednisolone was added. Cyanosis resolved and dyspnea slowly improved but she remained in impaired general condition and oxygen-dependent for 10 days. Her fever decreased after 9 days and on the 10th day pleural drainage was removed. The chest radiography showed expanded right lung with multiple small areas of opacity and several small areas of opacity in the left lung base. Methylprednisolone was stopped on the 10th day; meropenem and vancomycin were given for 14 days, then ceftriaxone for 7 days. On the 20th day she had moist rales in the right lung base and chest radiography showed a few small areas of opacity in the right lower lobe. She continued treatment with ciprofloxacin for 5 days and was discharged on the 28th day in good condition with normal blood tests and chest radiography. **Conclusion:** Pneumothorax and bilateral lung damage in acute hydrocarbons poisoning can be managed with immediate pulmonary drainage complete with complex and sustained medical treatment.[1] In severe cases chest radiography must be done, even early than 6 hours, repeated at 4–6 hours in the first 24 hours and then as frequently as necessary.[1]

## Reference

- [1] Gummin DG. Hydrocarbons. In: Nelson LS, Levin NA, Howland MA, et al., eds. *Goldfrank's Toxicologic Emergencies*. 9th ed. New York, USA: Mc-Graw Hill Medical; 2011:1386–1399.

## 280. Use of the paracetamol-aminotransferase product to predict hepatotoxicity in paracetamol overdose in a population treated with a two bag acetylcysteine regimen

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**Objective:** Risk prediction tools in paracetamol poisoning may help guide initial patient management and disposition. The paracetamol-aminotransferase multiplication product as a risk predictor is independent of time and type of ingestion, previously validated in a three bag acetylcysteine protocol.[1] The aim of this study was to evaluate the use of the multiplication product in an independent cohort of patients with paracetamol overdose treated with a two bag acetylcysteine regimen. **Methods:** We used a prospective dataset of poisoned patients presenting to 3 hospitals across Monash Health and identified all paracetamol overdoses from February 2014 to September 2015. We included all patients treated with acetylcysteine and excluded modified



release paracetamol ingestion. The acetylcysteine regimen consists of 200 mg/kg over 4 hours and 100 mg/kg over 16 hours. We assessed the diagnostic accuracy of the multiplication product (using first measured serum aminotransferase concentration and the simultaneous paracetamol concentration) for the outcome of hepatotoxicity (any ALT >1000 IU/L) at the pre-specified cut-off points of 1500 mg/L  $\times$  IU/L (10,000  $\mu$ mol/L  $\times$  IU/L) and 10,000 mg/L  $\times$  IU/L (66,000  $\mu$ mol/L  $\times$  IU/L). **Results:** Of 558 total paracetamol overdose presentations, 215 received acetylcysteine. This comprised 164 acute single, 10 delayed single (>24 hours post-overdose), 23 staggered (ingestion over >1 hour) and 28 supratherapeutic ingestions. Of these 16 patients developed hepatotoxicity: 4 acute single, 5 delayed single, 1 staggered and 6 supratherapeutic ingestions. Of all ingestions, 7 patients with a multiplication product >10,000 mg/L  $\times$  IU/L developed hepatotoxicity (likelihood ratio 18, 95% CI 7.4, 46.6), 5 patients with a multiplication product between 1500 and 10,000 (likelihood ratio 0.6, 95% CI 0.6, 1.2). No patient with a product <1500 mg/L  $\times$  IU/L who received acetylcysteine developed hepatotoxicity. **Conclusion:** Using a two-bag acetylcysteine infusion regimen, a product >10,000 mg/L  $\times$  IU/L was associated with a very high likelihood, and <1500 mg/L  $\times$  IU/L with a very low likelihood, of developing hepatotoxicity. This risk assessment is similar to that observed using a three-bag acetylcysteine regimen. The multiplication product should be considered more widely in risk-assessment of paracetamol-poisoned patients, particularly acute single ingestions presenting within 24 hours of exposure.

## Reference

- [1] Wong A, Sivilotti ML, Dargan PI, et al. External validation of a paracetamol-aminotransferase multiplication product used to predict hepatotoxicity in paracetamol overdose. *Clin Toxicol (Phila)*. 2015;53:807–814.

## 281. Use of the paracetamol-aminotransferase product to predict hepatotoxicity in modified-release paracetamol overdose

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**Objective:** Modified-release paracetamol tablets comprise 69% modified release and 31% immediate release paracetamol. In overdose, this can lead to late peak and prolonged elevation of the serum paracetamol concentration. The paracetamol-aminotransferase multiplication product as a risk predictor is independent of time and type of ingestion, previously validated in immediate-release paracetamol overdoses.[1] The aim of this study was to evaluate use of the multiplication product in a cohort of patients with modified-release paracetamol overdose. **Methods:** We used a prospective dataset of poisoned patients presenting to three hospitals across Monash Health and identified all paracetamol overdoses from October 2009 to September 2015, and included all patients who presented with modified-release

paracetamol ingestion. We assessed the diagnostic accuracy of the multiplication product (using first measured serum aminotransferase concentration and the simultaneous paracetamol concentration) for the outcome of hepatotoxicity (any ALT >1000 IU/L) at the pre-specified cut-off points of 1500 mg/L  $\times$  IU/L (10,000  $\mu$ mol/L  $\times$  IU/L) and 10,000 mg/L  $\times$  IU/L (66,000  $\mu$ mol/L  $\times$  IU/L). **Results:** Of 1478 total paracetamol overdose presentations, there were 68 modified-release paracetamol exposures. A product could be calculated in 58 cases of which 56 received acetylcysteine. This comprised 57 acute single, 2 delayed single (>24 hours post-overdose), 1 staggered (ingestion over >1 hour) and 8 supratherapeutic ingestions. Four patients developed hepatotoxicity: three acute single and one delayed single ingestion. An initial multiplication product >10,000 mg/L  $\times$  IU/L had a sensitivity of 100% (95% CI 39%, 100%) and specificity of 98% (88%, 99%). Four patients with an initial multiplication product >10,000 mg/L  $\times$  IU/L developed hepatotoxicity (likelihood ratio 54, 95% CI 7.7, 376.4). One of these patients had consumed 76 g of modified-release paracetamol and had acetylcysteine started 6 hours post-ingestion with normal transaminases, and a repeat product 8 hours later that was also >10,000 mg/L  $\times$  IU/L. No patient with a product <1500 mg/L  $\times$  IU/L developed hepatotoxicity. **Conclusion:** In the setting of modified-release paracetamol overdose, a product >10,000 mg/L  $\times$  IU/L was associated with a very high likelihood, and <1500 mg/L  $\times$  IU/L with a very low likelihood, of developing hepatotoxicity. Despite early presentation and treatment with acetylcysteine, a high initial product may predict hepatotoxicity, especially if it persists on repeat testing.

## Reference

- [1] Wong A, Sivilotti ML, Dargan PI, et al. External validation of a paracetamol-aminotransferase multiplication product used to predict hepatotoxicity in paracetamol overdose. *Clin Toxicol (Phila)*. 2015;53:807–814.

## 282. Detox, drugs and dialysis – do doctors follow the advice of a poisons centre? A prospective study of 206 cases in Northern Germany

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**Objective:** The first poisons centres were developed in Europe and North America in the second half of the twentieth century. Later, evidence-based medicine emerged and medical guidelines were published. The first publications on evidence-based clinical toxicology covered gastric lavage, activated charcoal and the use of several antidotes. The aim of this study was to explore the acceptance of poisons centres' advice in the professional medical field ("compliance"), i.e. did the doctors do what the poisons centre recommended? For this purpose a prospective study was designed and three questions were formulated: How often do doctors follow the recommendations of a poisons centre? Are there factors that influence the decision of the doctors? What is the overall satisfaction with the poisons centre? **Methods:** Cases were followed over a twelve month period (April 2010 to March 2011) and the following data were analyzed: sex and age of the patients, poisoning severity score, and the compliance of hospital doctors with regard to the recommendations of the poisons centre. **Results:** In total 206 cases were analyzed. Of these 61% of the patients were female, 39% were male. There were 5 age

**Table 1.** The frequency of procedures recommended by the poisons centre and doctors' compliance with the recommendation.

Procedure recommended by poisons centre	Frequency of recommendation	Frequency of recommendation that was followed
Gastric lavage	28	20 (71%)
Activated charcoal	56	48 (86%)
Dialysis	11	8 (73%)
Activated charcoal repeated	20	14 (71%)
Antidote (all)	53	39 (74%)
Acetylcysteine (paracetamol)	18	18 (100%)
Specific diagnostic procedures (all)	202	180 (89%)
Blood gas analysis	167	162 (97%)

categories. Compliance was highest in 2 groups: patients aged 1–4 years (86%) and >70 years (81%). The procedures that were recommended and the results are summarized in Table 1. Compliance was only 13% in cases where the doctor calling had difficulties with the German language, whereas the total compliance was 68%. The overall satisfaction with the poisons centre's service was 97%. **Conclusion:** The overall acceptance of the poisons centre's advice was excellent, with a satisfaction rate of 97%. Compliance ranged from acceptable to very good for most procedures. A problem group are doctors who call with only basic knowledge of the German language (compliance rate 13%). One solution could be faxing or emailing the relevant documents.

### 283. Inaccuracy of ECG conduction intervals and rhythm as reported to a Poisons Information Centre (PIC) after deliberate self poisoning

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**Objective:** Electrocardiographic (ECG) findings are used for diagnosis, prognosis and management decisions in poisoned patients. Cardiotoxic agents can interfere with cardiac conduction and cause arrhythmias, including torsades de pointes. Management decisions and escalation to a clinical toxicologist are often based on ECG characteristics. The objective of this study was to determine accuracy of ECG characteristics reported to a PIC by the treating clinician. **Methods:** This prospective observational study was conducted from May 2012 to February 2015 at a single PIC. All calls with requests for advice where an ECG was available and the treating clinician was able to verbally provide conduction intervals, rate and rhythm were enrolled. Results were recorded on preformatted study data collection sheets and ECGs were subsequently faxed to the PIC. Treating clinicians were blinded to the study objectives to minimize bias. All readable ECGs were analyzed separately by two clinical toxicologists blinded to the toxin(s) involved. **Results:** Initial enrolment consisted of 160 cases. Thirty were excluded, 18 due to poor ECG quality precluding interpretation and 12 because the ECG was not received. Overall there was very poor agreement between the ECG characteristics reported to the PIC and the reviewers' analyses. Agreement on underlying rhythm was obtained in only 32% of cases. Conduction interval durations were in agreement for QRS length in 85% and non-corrected QT interval in 20% of cases. Examples where reported parameters were thought to be clinically significant included reported QRS duration 110 ms, found to be 160 ms,

reported absolute QT interval 480 ms found to be 640 ms. Rhythm described as 4:1 atrioventricular (AV) block was found to be a sinus bradycardia, and reported as Wolff-Parkinson-White pattern was sinus rhythm in the opinion of both reviewers. Manual measurement of conduction intervals was completed in 21% of ECGs; 79% relied on ECG automated analysis. **Conclusion:** Reported ECG findings to the PIC correlate poorly with those as read by experienced clinical toxicologists.[1] This could be due to inexperience of the reader and reliance on automated ECG machine data. Electronic transmission of ECGs to clinical toxicologists providing remote clinical advice may improve the utility of this investigation in managing patients poisoned with cardiotoxic agents.

### Reference

- [1] Prosser JM, Smith SW, Rhim ES, et al. Inaccuracy of ECG interpretations reported to the poison center. *Ann Emerg Med.* 2011;57:122–127.

### 284. Unique histopathology in severe iron toxicity treated with liver transplantation

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**Objective:** Fulminant hepatic failure (FHF) from acute iron poisoning is uncommon, and infrequently requires liver transplantation. We describe FHF from acute iron overdose successfully treated with liver transplantation and report unique pathology of the native liver. **Case report:** A healthy 16-year-old girl presented to the emergency department with lethargy, abdominal pain, and bloody emesis approximately two hours after intentionally ingesting 54 × 325 mg iron sulfate tablets (70.2 mg/kg elemental iron) in a suicide attempt. She also ingested unknown amounts of ibuprofen-diphenhydramine and omeprazole. Her initial serum iron concentration was 311 μmol/L (1738 μg/dL); acetaminophen was undetectable. An abdominal radiograph was unremarkable and gastrointestinal decontamination was not performed. Despite prompt administration of intravenous deferoxamine, she developed coagulopathy, metabolic acidosis, and rising hepatic transaminases consistent with FHF within 24 hours post-ingestion. On day 3 post-ingestion, laboratory parameters peaked as follows: INR >13, ALT 12,466 IU/L, AST 11,400 IU/L, and total bilirubin 103 μmol/L (6.0 mg/dL). Serum creatinine remained normal. On day 4 she progressed to grade 4 hepatic encephalopathy, was endotracheally intubated, and received an emergent deceased donor liver transplant without intraoperative complication. Surgical pathology from the total hepatectomy specimen demonstrated massive acute panlobular hepatic necrosis with focal islands of residual hepatocytes showing intracanalicular cholestasis. There was diffuse centrilobular congestion and hemorrhage. Portal tracts contained mild to moderate lymphocytic infiltrates but lobules contained no significant inflammation. Remarkably, the iron stain was negative. Her post-operative course was complicated by fever, for which she received antipyretics and empiric antibiotics. On day 16 post-ingestion she was transferred to the inpatient psychiatric service. To date the patient continues to do well and routinely follows-up at liver transplant clinic. While iron overdose is relatively common, reports of FHF necessitating liver

transplantation are rare. This case of iron-induced FHF was successfully treated with liver transplantation and demonstrates unique explant pathology. Furthermore, iron is generally believed to be predominantly a peri-portal (zone 1) toxin, however significant centrilobular (zone 3) pathology was observed in this case. In addition, despite the significant overdose, the iron stain was negative. This also occurs after chelation therapy in other iron-overload states, such as hemochromatosis. Alternatively, the negative stain may be the result of significant hepatic necrosis and apoptosis of the hepatocytes. **Conclusion:** Liver transplantation can be a successful treatment for FHF secondary to acute iron toxicity. Further study is needed to elucidate the cause of this patient's hepatotoxicity and unique histopathology.

## 285. Topical aphrodisiac ingestion treated with digoxin-specific antibody fragments (DigiFab)

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**Objective:** Twenty years ago we first reported the use of digoxin-specific antibody fragments (Digibind) to treat bufadienolide-associated cardioactive steroid (CAS) toxicity resulting from ingestion of topical aphrodisiacs. We present two recent cases of severe CAS toxicity from topical aphrodisiac ingestion treated with a different digoxin-specific antibody fragment (DigiFab). **Case reports:** Case 1: A 49-year-old man presented with severe vomiting after unintentionally ingesting "Stone," a topical aphrodisiac. Vital signs were heart rate 26/minute, blood pressure 98/40 mmHg and respiratory rate 16 /minute. His electrocardiogram (ECG) demonstrated a junctional escape rhythm with a rate of 24/minute. Whole blood potassium was 4 mEq/L. He was treated empirically with ten vials of DigiFab due to concern for bufadienolide toxicity. Two hours later, his heart rate varied from 30–80/minute and potassium was 5.4 mEq/L. An additional ten vials of DigiFab were given with resultant normalization of heart rate (60/minute) and potassium (4.2 mEq/L). Six hours later, his heart rate decreased again to 36/minute and potassium rose to 6.1 mEq/L. He received a final ten vials of DigiFab and activated charcoal, after which he continued to improve. He was discharged on hospital day three without sequelae. Case 2: A 39-year-old man presented with vomiting and diaphoresis following erroneous ingestion of "Piedra China," a topical aphrodisiac. Vital signs were heart rate 65/minute, blood pressure 157/66 mmHg and respiratory rate 20/minute. Shortly after arrival, ECG revealed sinus bradycardia (45/minute) with atrioventricular (AV) dissociation. Serum potassium was 4.6 mEq/L and apparent digoxin concentration was 1.45 nmol/L (1.14 ng/mL). He acutely deteriorated; ECG showed paroxysmal atrial tachycardia with 3:2 conduction, which progressed to ventricular fibrillation. He underwent 90 minutes of resuscitation and was treated with defibrillation, epinephrine, atropine, amiodarone, procainamide and repeated boluses of DigiFab. After each dose of antidotal therapy (10 vials, 12 vials, and 11 vials respectively) his rhythm converted to normal sinus (heart rate 70–80/minute) with return of spontaneous circulation. Unfortunately, these improvements were transient and despite aggressive care the patient suffered another arrest and progressed to asystole in the absence of additional antidote. **Conclusion:** Bufadienolides are extremely potent CASs present in toad venom and persistently sold as topical aphrodisiacs. Large dose DigiFab therapy seemed to be an effective treatment,

as reported previously with Digibind. Insufficient gastrointestinal decontamination and/or inadequate antidotal therapy due to supply limitations likely contributed to the death of our second patient.

## 286. TOXIC study: exposures and outcome of intoxicated patients visiting the emergency department

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**Objective:** A considerable number of emergency department (ED) visits are due to intoxications. Outcome of these patients, other than admission rates, is largely unknown. Therefore, this study aimed to characterize these patients, their exposures and their outcome. **Methods:** Patients who visited the ED of the University Medical Center Utrecht, the Netherlands, due to an (suspected) intoxication between 1 January 2015 and 31 July 2015 were included in the study. Data were collected prospectively from electronic patient files and included data on specific exposures and the clinical course. The observed severity of the intoxication was determined using the Poison Severity Score (PSS). In addition, telephone questionnaires and toxicological analysis of left-over blood samples were performed. **Results:** In total 189 patients were included in the study, comprising 1.4% of the total ED population. The average age was 34 years and gender was equally distributed. The majority of the patients had one or more co-morbidities (70%); 30% had a somatic co-morbidity and 64% had a psychiatric co-morbidity. Over half of the patients were exposed to  $\geq 1$  substance based on anamnesis. Reported exposures mostly involved pharmaceuticals, pharmaceuticals combined with ethanol, only ethanol, only illicit drugs and illicit drugs combined with ethanol. A qualitative screening for drugs of abuse in urine was performed in 66% of the patients and was positive most frequently for benzodiazepines, followed by cannabis. Broad qualitative analysis will be performed to evaluate the correlation between exposures reported by patients and measured exposures. The majority of patients were admitted (60%), mostly to the department of Internal Medicine and 4% to the Intensive Care Unit. More than half of the patients presenting with an intoxication to the ED had a mild intoxication (at the ED or ward) based on the PSS. Of these mildly intoxicated patients, approximately 50% were admitted. **Conclusion:** Intoxicated patients contribute considerably to ED visits in our hospital and many of these patients are admitted. Poison Centres can provide an expected PSS and aid in triage and treatment of intoxicated patients, as our data showed that patients with a mild intoxication were often admitted. However, the observed severity could be underestimated, since treatment was not included in the PSS assessment. Our data will be used to evaluate the applicability of broad toxicological analyses in the treatment of intoxicated patients and to develop models to predict which patients should be admitted and which can be discharged.

## 287. Mathematical modelling of the effect of a high dose acetylcysteine regimen based on the SNAP trial on hepatic glutathione regeneration and hepatocyte death

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**Objective:** A novel acetylcysteine ("SNAP") regimen (100 mg/kg over 2 h then 200 mg/kg over 10 h) causes fewer adverse reactions.[1] Although likely to be effective in most patients, more prolonged therapy will be needed in those with substantial paracetamol overdose.[2] This could be achieved by administration of a further 200 mg/kg infusion over 10 hours (total 500 mg/kg over 22 hours). We aimed to compare the effect on hepatic glutathione regeneration and hepatocyte death of this extended 22 hour SNAP regimen with the standard 12 hour SNAP regimen and the current UK acetylcysteine regimen (150 mg/kg over 1 hour, 50 mg/kg over 4 hours then 100 mg/kg over 16 hours, total 300 mg/kg over 21 hours). **Methods:** A published mathematical model integrating a model of paracetamol transport and metabolism with a model of glutathione metabolism [3] was used to simulate the effects of acetylcysteine on glutathione regeneration and functional hepatocyte numbers. These were compared between the three regimens evaluated. **Results:** Hepatic glutathione regeneration was predicted to occur earlier and the nadir of functional hepatocytes was predicted to be higher with the 22 hour extended SNAP regimens compared to the currently used and 12 hour SNAP regimens. Hepatic glutathione generation occurred latest and the nadir of functional hepatocytes was lowest with the 12 hour SNAP trial regimen. However, the nadir of functional hepatocytes exceeded 40% with all three regimens suggesting that they were all effective in preventing hepatic failure which is generally associated with 20–30% hepatocyte function. **Conclusion:** Although most patients at lower risk will be treated effectively by the 12 hour SNAP regimen, those with more substantial overdose will require higher dose and more prolonged therapy. This can be achieved by repeating the 10 hour (200 mg/kg) infusion in those at risk, e.g. those with persisting plasma paracetamol concentrations or evolving liver function abnormalities after the initial 12 hour regimen. Further studies are required to evaluate the clinical efficacy of this approach.

### References

- [1] Bateman DN, Dear JW, Thanacoody HKR, et al. Reduction of adverse effects from intravenous acetylcysteine treatment for paracetamol poisoning: a randomized controlled trial. *Lancet*. 2014;383:697–704.
- [2] Bateman DN, Dear JW, Thanacoody HKR, et al. Treatment of paracetamol overdose - authors' reply. *Lancet*. 2014;383:1383.
- [3] Ben-Shachar R, Chen Y, Luo S, et al. The biochemistry of acetaminophen hepatotoxicity and rescue: a mathematical model. *Theor Biol Med Model*. 2012;9:55.

## 288. Massive accidental caffeine overdose treated with continuous veno-venous haemodiafiltration (CVVHDF)

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**Objective:** We report two students who developed severe acute toxicity following ingestion of caffeine following a one thousand-fold dose calculation error during a university experiment. Both required critical care admission and underwent CVVHDF with the aim of enhancing caffeine elimination, as a previous report had suggested benefits from haemodialysis.[1] **Case report:** Case 1: A 20-year-old male ingested 30 g caffeine and developed nausea, haematemesis, agitation, tremor, diarrhoea, hypertension (171/71 mmHg), QTc prolongation (586 ms, heart rate 84 bpm), neutrophilia ( $14.23 \times 10^9/L$ ), hypokalaemia (2.7 mmol/L), elevated ALT (163 U/L) and lactate (6.9 mmol/L), mild compensated metabolic acidosis (pH 7.39, bicarbonate 20 mmol/L) and rhabdomyolysis (peak creatine kinase 6891 U/L 29 hours post-ingestion). Blood pressure and QTc interval normalised over the first 24 hours. CVVHDF was used between 9 hours and 45 hours post-ingestion. Case 2: A 20-year-old male ingested 30 g of caffeine and developed nausea, haematemesis, tremor, blurred vision, epigastric pain, diarrhoea, hypotension (94/69 mmHg), QTc prolongation (536 ms, heart rate 64 beats/min), neutrophilia ( $9.43 \times 10^9/L$ ), hypokalaemia (2.4 mmol/L), elevated creatine kinase (1369 U/L) and lactate (6.9 mmol/L) and compensated metabolic acidosis (pH 7.39, bicarbonate 18 mmol/L). Cardiac monitoring revealed multifocal premature ventricular contractions and non-sustained runs of ventricular tachycardia for which he received IV magnesium (4 mg). He also received IV diazepam for agitation, ondansetron for nausea, omeprazole for gastric protection and potassium replacement. He developed severe hypertension with a systolic blood pressure 190 mmHg requiring glyceryl trinitrate and labetalol infusions on days 2 and 3 and oral metoprolol on day 3. He also required fentanyl analgesia for abdominal pain. Creatine kinase peaked 27 hours post-ingestion (14,717 unit/L). CVVHDF was used between 7.3 hours and 69 hours post-ingestion; at this point his lactate had normalised and his initial ALT of 31 U/L peaked at 166 U/L 75 hours post-ingestion. Analysis of blood samples revealed peak caffeine concentrations of 366.8 and 352.3 mcg/mL, respectively. Apparent caffeine half-lives during CVVHDF were 4.9 hours and 7.8 hours, respectively. **Conclusion:** Two young males with potentially lethal caffeine intoxication survived with supportive care. CVVHDF was also used but half-lives during this were not reduced compared to published values without enhanced elimination methods (4–6 hours), although prolongation of half-life (up to 16 hours) after overdose has been reported. These data do not suggest benefit from CVVHDF, but further studies with clearance data are needed.

### Reference

- [1] Fausch F, Uehlinger DE, Jakob S, et al. Haemodialysis in massive caffeine intoxication. *Clin Kidney J*. 2012;5:150–152.

## 289. Pneumobilia as a complication of accidental ingestion of methyl ethyl ketone peroxide

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**Objective:** Methyl ethyl ketone peroxide (MEKP) is a colorless, odorless organic compound used in industrial processes as a catalyst, in diluted solution (30–60%). When ingested, MEKP causes direct caustic injuries by oxygen free radical production. With metal ions, MEKP readily forms alkyl and/or peroxy radicals inducing lipid peroxidation of digestive tract and liver. Massive ingestion of MEKP may induce acute liver failure, which is the major cause of death. Finally, during MEKP decay, various organic acids are formed, e.g. formic acid, which induce acidosis and optic neuropathy. Symptoms of acute MEKP poisoning include gastrointestinal burns and bleeding, esophageal and gastric perforation, severe metabolic acidosis, rapid hepatic failure, rhabdomyolysis and respiratory failure. As with all peroxides, MEKP may produce high volumes of oxygen which could lead to gastrointestinal distension. **Case report:** A 47-year-old man was admitted to the Emergency Department of Monfalcone Hospital, after ingesting a liquid from an unlabeled bottle which was mistaken for water but contained MEKP 60%. On admission he had severe epigastric and chest pain. Vital signs were normal. No oral lesions were present but he experienced vomiting and drooling. Intravenous fluids, atropine 0.5 mg, metoclopramide 10 mg, morphine 10 mg and pantoprazole 80 mg (followed by 2 g in 24 hours), were administered. Chest and abdomen computerised tomography (CT) scan, performed after discussion with the Florence Poison Control Center, showed a massive pneumobilia associated with distention of jejunum-ileus because of oxygen production. Esophagogastroduodenoscopy (EGDS) was performed to assess the severity of the caustic injury. Esophageal mucosal oedema (grading 1 Zargar's score) and several gastric necrotic areas (grading 3a) were present. The duodenum revealed few scattered superficial erosions. The surgeon decided for non-surgical treatment of pneumobilia and gastric injuries. The patient underwent orotracheal intubation and was transferred to an intensive care unit. Two days later, endoscopic examination was performed. Pneumobilia spontaneously recovered in 6 days. The patient was discharged after 15 days and EGDS follow up was prescribed. **Conclusion:** Pneumobilia, typically visualized as a large air confluence within the central portion of the liver, can be a complication of endoscopic or surgical procedures involving the biliary tract. To our knowledge, this is the first case of MEKP-induced pneumobilia. The patient developed local damage but limited systemic effects with a favorable outcome. Therefore, MEKP could be lethal upon ingestion and intoxicated patients should be followed for the risk of unexpected organ injury.

## 290. Severe toxicity with guanidine thiocyanate ingestion: a case report

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**Objective:** Commercially guanidine thiocyanate is used as a protein denaturant and in the extraction of DNA and RNA. There are no reports of its toxicity from oral ingestion however thiocyanate toxicity has been described in the context of cyanide toxicity from nitroprusside in the setting of renal impairment.[1] A drug review of nitroprusside pharmacokinetics reports thiocyanate has a half-life of 2.7 days and almost 100% renal clearance.[2] We report a case of deliberate guanidine thiocyanate ingestion and its treatment, including dialysis. **Case report:** A previously well 52-year-old male biochemist presented to a peripheral hospital with a history of crampy abdominal pain after drinking bottled water that he reported tasted odd. His initial vital signs were normal, however while undergoing investigation he became confused and agitated. This required sedation, intubation and ventilation with subsequent transfer to a tertiary hospital intensive care unit for ongoing care. A computed tomography (CT) scan of his brain and abdomen were unremarkable. He had an unmeasurable chloride (error reading) and a low ionized calcium of 0.59 mmol/L (1.15–1.32 mmol/L) on an arterial blood gas with a normal serum total calcium. The remainder of his biochemical and haematological investigations were normal. A urine drug screen was negative. He was managed initially with intravenous calcium. An analysis of the water for electrolytes gave discrepant chloride readings on two laboratory chemistry analysers suggesting a cross reacting analyte.[3] Further analysis revealed this to be thiocyanate with a serum concentration on admission of 538 mg/L (0.1–4.0 mg/L in non-smokers). Continuous veno-venous haemodialysis was commenced based on this concentration and known long half-life. Five pre-dialysis serum samples demonstrated zero-order elimination pharmacokinetics. Nine post-dialysis serum samples demonstrated first-order kinetics with an elimination half-life of 5.8 hours. The patient made a full recovery and admitted to deliberate addition of guanidine thiocyanate to the bottled water. **Conclusion:** This is the first report of guanidine thiocyanate poisoning causing neurological toxicity, hypocalcaemia and discordant chloride readings. Dialysis has a role in the treatment of its toxicity.

### References

- [1] Nessim SJ, Richardson RMA. Dialysis for thiocyanate intoxication: a case report and review of the literature. *ASAIO J.* 2006;52:479–481.
- [2] Schulz V. Clinical pharmacokinetics of nitroprusside, cyanide, thiosulphate and thiocyanate. *Clin Pharmacokinet.* 1984;9:239–235.
- [3] Dimeski G, Kruger P, Walsham J. Unmeasurably high chloride: a surrogate marker of thiocyanate poisoning identification. *Clin Chem Lab Med.* 2015;53:e151–e152.

## 291. Cost and availability of intravenous lipid emulsion therapy: a worldwide survey

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**Objective:** The American Academy of Clinical Toxicology created a workgroup composed of international experts from various clinical specialties to produce systematic reviews and to formulate evidence-based recommendations on the use of intravenous lipid emulsion (ILE) in poisonings. In order to balance the risk and benefit ratio, an evaluation of the costs of ILE from various countries was studied. **Methods:** An online survey was sent out from October 2014 to June 2015 to clinicians worldwide via the membership email distribution list of several clinical toxicology associations. **Results:** There were a total of 56 responders. Data of ILE cost and availability could be extracted from 53 responders in 20 countries. All responders had lipid emulsion formulation available in their workplace. The breakdown of ILE availability was the following: 95% of responders had access to Intralipid 20%, 60% of responders had access to Clinoleic 20%, 20% of responders had access to Intralipid 10%, and 20% of responders had access to Intralipid 30%. Costs were converted to USD currency and calculated per 100 mL. The mean costs of ILE for each country for which data was available was used to calculate the median international costs of ILE. Median costs were the following: Intralipid 20% = \$5.60 (IQR \$3.15–\$9.99), Clinoleic = \$7.01 (IQR \$3.60–\$9.31), Intralipid 10% = \$3.99 (IQR \$2.20–\$7.36), Intralipid 30% = \$7.75 (IQR \$6.04–\$8.74). **Conclusion:** The results of this survey suggest that ILE is an inexpensive treatment and is readily available worldwide.

## 292. Emergency Department (ED) visits, hospital admissions, and deaths managed by the Hawaii Poison Center (HPC): 2010–2014

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**Objective:** We wished to determine the percentage of poisoned patients in Hawaii who died, were admitted to hospital or seen in the emergency department (ED) managed by the Hawaii Poison Center (HPC). Additionally, we explored the feasibility of linking HPC calls, Emergency Medical Services (EMS) pre-hospital and hospital case data to better understand the relationships between these datasets. **Methods:** We compared aggregate death certificate and EMS pre-hospital data and HPC data for deaths and non-iatrogenic hospital treatments for poisonings and envenomations for 2010–2014. We tabulated HPC contacts for closed human exposures by Generic Code Category, Medical Outcome, Management Site and Level of hospital care from the National Poison Data System (NPDS) by year. **Results:** Poisoning accounted for 14,515 ED visits and 3770 Admissions (12% of all non-iatrogenic injury hospitalizations) (Table 1). The percentage managed by the HPC were 36% ED visits, 74% Admissions, and 3.2% deaths. Pharmaceuticals accounted for 92% of the 880 deaths and 83% of the deaths managed by the HPC. **Conclusion:** Over the study period, poisonings were the leading mechanism of injury-related mortality in Hawaii, surpassing deaths from motor vehicle crashes and falls. A direct linkage of HPC, EMS records and hospital medical records could provide evidence of value added (length of stay, charges, discharge status, etc.) by HPC management. Such linkage could be accomplished by using a third party non-profit organization that maintains billing data abstracts from all Hawaii, non-federal acute care hospitals, using common data elements such as patient details, and date and time of exposure. A current project has linked 85% of the records

**Table 1.** Poisoning cases in Hawaii 2010–2014 comparing data from the Emergency Medical Services (EMS) and the Hawaii Poison Center (HPC).

Level of care/Deaths	2010–2014		Cases per year		Proportion handled by the HPC
	EMS	HPC	EMS	HPC	
ED visits	14,515	5174	2903	1035	36%
Hospital admissions	3770	2804	754	561	74%
Deaths	880	28	176	5.6	3.2%
From pharmaceuticals	810	24	162	4.8	3.0%
From non-pharmaceuticals	70	4	14	0.8	5.7%

of EMS-transported patients to corresponding hospital admissions. Linking HPC data to EMS and hospital admission records is the next step. Linked data could support a quantitative evaluation of the effectiveness HPC intervention in improving the outcomes of poisoned patients.

## 293. Bath salts (synthetic cathinones): two cases with forensic implications

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**Objective:** The use of recreational drugs, also called legal highs, has been increasing, particularly due to easy access via the Internet. In 2009 and 2010, a significant rise in the abuse of a new group of synthetic cathinones (“bath salts”) was reported in Western Europe. We present two cases of exposure with complete identification of substances in biological samples. **Case reports:** Case 1: A 19-year-old male with a history of cannabis use from the age of 17 was arrested for assaulting his father during a family argument. He had gone to a party and did not ingest anything except half a bottle of rum and some beer plus the content of an abandoned glass from a shelf. Soon after he felt unwell and described a feeling of elation, irritability, and episodes of amnesia. He presumed there was something in the drink, and in his words suspected “MD” or something similar. He had a daily consumption of 1 g smoked cannabis and occasionally consumed “MD”. 11-nor- $\Delta^9$ -tetrahydrocannabinol-carboxylic acid and methylene (3,4-methylenedioxy-N-methylcathinone) were detected in urine. Case 2: The decedent was a Caucasian, athletic 33-year-old male found hanging in his bathroom. There was no information on substance abuse or suicidal ideation or gesture. The medical examiner reported the cause of death as hanging and based upon the examination of the scene and the anatomopathological data the manner of death was determined to be suicide. Alpha-pyrrolidinovalerophenone (alpha-PVP, street name Flakka) and 4-methylethcathinone (4-MEC) were found in blood and urine. Cocaine and its metabolites were found in a urine sample. All drugs and metabolites were detected using gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS). **Conclusion:** These cases highlight the severe toxicity including behavioral abnormalities and self-harm induced by easily accessible drugs such as synthetic cathinones. Their analytical detection is an increasingly serious challenge faced by toxicologists due to the increasing number of compounds that appear constantly in the illicit market and the necessity of having modern laboratories with very sensitive and highly specific instrumental analytics. In the first case a limitation was the patient who was the only source of information and had compromised reliability;

although the case also exemplifies that a complete history from the relatives is important in the evaluation of any individual who presents with bizarre or unexpected behavior.

## 294. The toxicological significance of drug concentrations in bile

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**Objective:** Clinical toxicologists are used to interpreting blood concentrations. Standard texts of toxicological analysis list blood and bile concentrations. This systematic review examined whether bile concentrations reflected blood concentrations post-mortem. **Methods:** EMBASE was searched from 1980–2015, using the terms 1. bile/ or exp drug bile level/ AND 2. Drug blood level/; MEDLINE from 1990–2015, using the terms 1. exp Bile/ AND 2. exp [drug name]/bl,pk,po; and the indexes of relevant journals were searched. The variability of the bile: blood concentration ratio was examined. **Results:** From 650 titles, 110 potentially relevant papers were retrieved; 24 gave information on drugs (Table 1). Four papers quoted mean ratio  $\pm$  standard deviation for ethanol; the overall mean ratio was approximately 1.0 (95% CI 0.4–2.0). **Conclusion:** “Bile is not commonly used as a specimen in routine toxicological analysis,” [1] but “serves as an excellent site for drug identification for drugs that are found in high concentrations in the liver.” [2] This is important for qualitative detection of drugs in forensic toxicology, however, if bile concentrations are to be quantitatively useful, then bile: blood concentration ratios must be well defined to allow deduction of one from the other. Previous reports, based on few cases, [3,4] have suggested this may be possible. The highly skewed values and wide ranges found here show this is not so. Bile concentration measurements cannot be used to establish ante-mortem blood concentrations.

### References

- [1] Agarwal A, Lemos N. Significance of bile analysis in drug-induced deaths. *J Anal Toxicol.* 1996;20:61–63.
- [2] Leikin JB, Watson WA. Post-mortem toxicology: what the dead can and cannot tell us. *J Toxicol Clin Toxicol.* 2003;4:47–56.
- [3] Bévalot F, Cartiser N, Bottinelli C, et al. Correlation of bile and vitreous humor concentrations with blood drug concentrations for forensic interpretation: a comparative study between animal experimental and human postmortem data. *Forensic Toxicol.* 2015;33:131–140.
- [4] Vanbinst R, Koenig J, Di Fazio V, et al. Bile analysis of drugs in postmortem cases. *Forensic Sci Int.* 2002;128:35–40.

**Table 1.** The bile: blood ratio for a variety of drugs.

Compound	Bile: blood concentration ratio	
	Median	Range
Citalopram ( $n \approx 30$ )*	9.0	6.0–1088
Codeine ( $n = 6$ )	3.9	0.3–25.5
Duloxetine ( $n = 4$ )	11	3.5–22
Fentanyl ( $n = 14$ )	3.6	1.1–11
Fluoxetine ( $n = 6$ )	9.0	6.0–29
Mirtazapine ( $n = 4$ )	9.9	6.4–15
Morphine ( $n = 113$ )	36	0.5–3500
Phencyclidine ( $n = 15$ )	2.0	0.25–10
Quetiapine ( $n = 18$ )	10	5.0–186
Trazodone ( $n = 4$ )	1.6	1.0–2.9

\*Precise number unascertainable

## 295. Synthetic cannabinoid MDMB-CHMICA identification in illegal products

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**Objective:** MDMB-CHMICA is a new cannabimimetic indole derivative used in a smoking blend on the Serbian market. This report presents a method of its analysis in herbal products. **Methods:** Packages of herbal blends, with brand names “Sharp” and “Luminated” and cigarettes containing unidentified herbal mixtures, were analyzed. In samples, MDMB-CHMICA was detected by liquid-liquid extraction of methanol. The structure of this compound was identified by gas chromatography-mass spectrometry (GC-MS), high-resolution MS, using GC-Ion-Trap-MS system equipped with a Thermo TG-5MS capillary column. The injector was operated in split mode (50:1) at 260 °C. Helium gas was used as the carrier gas at flow rate of 1.0 mL/min. The oven temperature was held at 100 °C for 1 min and ramped to 300 °C at a rate of 12 °C/min and held for 9 min. The MS conditions were as follows: transfer line heater 200 °C and ion source temperature 220 °C. The injection volume was 1  $\mu$ L. [1] **Results:** After GC-MS analysis of the “herbal mixture” peaks were identified with its major ion signals at  $m/z$  240, 328, 144, 384 as MDMB-CHMICA. **Conclusion:** Herbal products containing synthetic cannabinoids often change qualitatively and quantitatively, making it difficult for laboratories to remain current. We detected MDMB-CHMICA as the major psychoactive ingredient in some herbal mixtures and cigarettes sold on our market. We consider the described method suitable for the detection of MDMB-CHMICA.

### Reference

- [1] Uchiyama N, Matsuda S, Kawamura M, et al. Two new-type cannabimimetic quinolinyl carboxylates, QUPIC and QUICH, two new cannabimimetic carboxamide derivatives, ADB-FUBINACA and ADBICA, and five synthetic cannabinoids detected with a thiophene derivative  $\alpha$ -PVT and an opioid receptor agonist AH-7921 identified in illegal products. *Forensic Toxicol.* 2013;31:223–240.

## 296. The role of the toxicology laboratory in the risk assessment of toxicity from counterfeit herbal products

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**Objective:** In Morocco, some herbal products are freely sold in the markets and often escape regulatory control. The Poison Control and Pharmacovigilance Centre of Morocco (CAPM) contributes, as part of its toxicovigilance role, to the risk assessment of such products. The confirmation of their hazard is performed at the laboratory of the CAPM. Our aim is to highlight the role of the toxicology laboratory in risk assessment of counterfeit products. **Methods:** We report two types of herbal products sold on the black market and another sold by herbalists without labeling that have been the subject of information requests to the pharmacovigilance department. The analysis of the three products was performed by high performance liquid chromatography and gas chromatography coupled to mass spectrometry. **Results:** The first product, imported from Indonesia called "Labaik" is indicated in the treatment of several diseases and symptoms including arthritis, rheumatism, insomnia, fatigue and hypercholesterolemia. The results of the laboratory have shown that the compounds in this product are paracetamol, phenylbutazone, methyl-aminophenazone and noramidopyrine. Obviously the adulterated chemicals are not shown in the list of ingredients. The second product is an herbal mixture for obesity and to promote weight loss. The results of the laboratory have shown that this product contains phenols and terpenes without medicines or pesticides. The third product is a herbal syrup sold by herbalists to women and children in order to increase appetite for weight gain. The product analysis has found it contained an antihistamine, cyproheptadine. Once these results were communicated to the staff of the pharmacovigilance centre, a consumer awareness strategy was implemented and an alert was published in the journal of the CAPM. **Conclusion:** The toxicology laboratory actively contributes to the assessment of risks related to the sale of counterfeit products and participates in the health surveillance process.

## 297. Ingestion of liquid fertilizer as suspected cause of death

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**Objective:** Liquid fertilizer for domestic use is considered safe and rather harmless after unintended intake. Suicide attempts, however, comprise a significant risk but are seldom reported in the literature. We report a fatal case. **Case report:** A 45-year-old woman with a history of a previous suicide attempt was found lifeless in bed in the morning. Resuscitation was unsuccessful. She was last seen alive 55 minutes earlier. Beside the bed were found two empty vials of chlordiazepoxide (100 × 25 mg), a suicide note and a three liter bottle of liquid fertilizer (Greenworld<sup>®</sup> liquid fertilizer, Denmark). The ingredients were nitrogen compounds 7% (including ammonium 2%, nitrate 2% and urea 3%), phosphorus 3.3% and potassium 5% (as potassium chloride). Approximately 750 ml of the content was missing. The medical history included pathology related to alcohol, but no lethal conditions. At autopsy the external and internal examinations showed no identifiable

anatomical cause of death. Gastric contents included 600 ml of fluid. Toxicological analysis in femoral blood determined lithium 1.8 mmol/kg, chlordiazepoxide 0.27 mg/kg, zopiclone 0.016 mg/kg and salicylic acid 11 mg/kg. No ethanol was detected. Gastric content was found to contain high concentrations of nitrite, nitrate, sulphate and phosphate. There was no difference in the levels of cations such as potassium, sodium and ammonium compared with gastric content from a normal control person. **Conclusion:** Anatomical examination and toxicological analysis of blood revealed no obvious cause of death. The concentrations of psychoactive substances were below toxic concentrations. The bottle with fertilizer was beside the bed in the morning, and had not been used and it is likely she had ingested the missing volume; 750 ml of 5% potassium contains 37.5 g potassium (960 mmol). With a weight of 60 kg, she had taken 16 mmol/kg of readily absorbed potassium chloride. The high concentration of nitrates, sodium and ammonium in the stomach is consistent with ingestion of fertilizer. The absorption rate of these electrolytes is slower than potassium due to the smaller concentration gradient. The normal concentration of potassium in the gastric fluid may be explained by rapid absorption of potassium. Post-mortem potassium leaks out of cells, making potassium concentrations unreliable minutes after death. Therefore, although we are not able to prove the cause of death in this case, we consider potassium from the fertilizer a reasonable reason.

## 298. "Spiked" urine in buprenorphine-assisted treatment of opioid dependence: the quantification of metabolites allows for detection of adulteration

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**Objective:** Buprenorphine is available alone or co-formulated with naloxone, most typically in a 4:1 ratio as tablets or strips to be administered sublingually for the treatment of opioid dependence. Buprenorphine preparations reduce craving, prevent withdrawal, and have a "blocking" effect when other opioids are used concomitantly. Despite some evidence showing it is less abused than other opioids there is still substantial diversion of buprenorphine. Providers that treat opioid-dependent patients with buprenorphine must be familiar with methods for detecting diversion in order to be most effective in their practice and to minimize any harm associated with inappropriate use of buprenorphine. A case of urine adulteration is presented in order to highlight the importance of obtaining and quantifying urine buprenorphine and metabolite concentrations in order to detect non-compliance and limit diversion. **Case report:** A 47-year-old male with opioid dependence entered into drug treatment as a condition of parole. He was started on a buprenorphine/naloxone formulation at 8/2 mg sublingual twice daily and was doing well with good attendance and participation reports from his counseling and group sessions. His urine consistently showed buprenorphine concentrations <3 ng/mL with norbuprenorphine/creatinine ratios of 600–800 ng/mg creatinine during this time. Unfortunately, after a couple of months he started to show up late and disorganized and then started to miss groups entirely. His urine drug testing was noted to be markedly different from earlier samples (buprenorphine >4000 ng/mL with norbuprenorphine/creatinine concentrations non-detectable). A repeat urine sample was obtained under direct observation and 6-monoacetylmorphine and cocaine but no buprenorphine or metabolites were present. The patient



admitted to spiking a friend's urine with the buprenorphine/naloxone preparation and turning this in in lieu of his own urine due to his relapse and return to illicit heroin use. **Conclusion:** Buprenorphine is metabolized to norbuprenorphine and conjugated to buprenorphine and norbuprenorphine glucuronide products during normal metabolism. These metabolites are excreted in the urine. Norbuprenorphine is often standardized to the urine creatinine in order to obtain a concentration which is not affected by dilution. High buprenorphine (>4000 ng/mL) and negligible metabolite concentrations, with naloxone in the urine (buprenorphine/naloxone formulation), suggests the medication did not pass through the patient before being present in the urine. He admitted this when confronted with the results. Urine buprenorphine and metabolite quantification allows for differentiation between adulterated/spiked urine and normal metabolite profiles.

## 299. Accidental poisoning with pulverized *Veratrum*: a case report with analytical confirmation

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**Objective:** *Veratrum* has been used in traditional medicine in Europe, Asia and America for various conditions such as sore throats, snake bites, wounds, dysentery and apoplexy. Until the 1960s *Veratrum* alkaloids were also used as antihypertensive drugs. Pulverized *Veratrum album* rhizomes were marketed as sneezing powder causing several incidents of serious toxicity until the 1980s. *Veratrum* alkaloids of the veratramine and jervine-type bind to voltage-gated sodium channels, augmenting cell wall permeability to cations such as sodium and calcium and resulting in cell excitability. A single stimulus then causes multiple depolarisations of neurons and muscle cells. The vagal nerve is typically involved. Symptoms occur within 0.5 to 4 hours with initially nausea, vomiting, abdominal pain and diarrhoea. Cardiotoxic symptoms of vagal overstimulation include hypotonia and bradycardia. In serious cases repolarisation abnormalities (negative T waves, ST segment shifts, supraventricular blocks, lengthened QT) are observed. Neurological signs include headache, vertigo, sweating, paraesthesia, delirium, sleepiness and convulsions. Therapy is supportive and in cases with signs of vagal overstimulation atropine can be given. Outcome is usually favourable.[1] **Case report:** A 76-year-old woman with diabetes mellitus accidentally drank a slurry containing 1 teaspoon of dry powdered *Veratrum* in water. Within 30 minutes she experienced nausea, vomiting, abdominal pain, diarrhoea and general weakness. On admission to hospital she complained of abdominal pain, nausea and facial and digital paresthesia. She had slurred speech and appeared somnolent but oriented; systolic blood pressure was 90 mmHg, pulse 46/min with first degree atrioventricular block (AV) block. Laboratory tests were normal. After 12 hours of supportive care she was asymptomatic and the electrocardiogram (ECG) had normalized. Qualitative toxicological analysis by high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) of the patient's serum (from admission), urine (after 12 hours) and the alleged plant powder found three alkaloids (protoveratrine A, protoveratrine B and jervine) in urine, serum and powder. A fourth alkaloid, veratridine, was detected in urine and powder, but not in serum. **Conclusion:** We report a case with analytical confirmation of oral intoxication with *Veratrum*. The patient

developed symptoms of toxicity within 30 minutes which subsided within 12 hours with supportive care. Three alkaloids (protoveratrine A and B and jervine) were detected in the patient's serum and urine. In addition veratridine was found in urine. All four alkaloids were detected in the powder.

## Reference

- [1] Schep LJ, Schmierer DM, Fountain JS. Veratrum poisoning. *Toxicol Rev.* 2006;25:73–78.

## 300. *Amanita phalloides* ingestion in children in Austria, 1996 to 2014

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**Objective:** Mushroom ingestions are frequent reasons for contacting the Austrian Poisons Information Centre (PIC). The mushroom hunter's levels of experience vary widely and in some cases, due to lack of knowledge it is possible that the dangerous *Amanita phalloides* can be ingested. We examine the cases of mushroom ingestion in children reported to the PIC and describe two cases of *Amanita phalloides* ingestion requiring liver transplantation. **Methods:** Cases of mushroom ingestion, including those involving *Amanita phalloides*, in children were evaluated based on the PIC database from 1996–2014. **Results:** In the 19 year study period the PIC in Austria received 1072 telephone enquiries regarding mushroom ingestion in children (39 less than 1 year old, 664 aged 1–6 years, 267 aged 6–14 years and 102 with age unknown). In 733 children (68%) only a small amount of a single mushroom was ingested. Of these cases medical care was recommended in 31 children (4.3%) due to suspicion of intoxication. *Amanita phalloides* was verified in 12 (1.6%) of 733 cases. No child developed symptoms. In 339 cases (32%) mushrooms were consumed as part of a meal. Observation at hospital was recommended in 93 children (27.5%). *Amanita phalloides* was verified in 12 (3.5%) of 339 cases. In three cases no symptoms occurred due to early consultation. The remaining children developed gastrointestinal symptoms, three developed hepatic impairment and two children had liver transplantation, one of them died. Case 1: A 16-month-old boy was fed mushrooms in a meal. The child developed diarrhoea and vomiting and was hospitalized. Medical therapy was started more than 20 hours after ingestion. On the following days hepatic impairment was diagnosed and molecular adsorbent recirculating system (MARS) was used due to liver failure. Despite liver transplantation the child died 9 days after *Amanita phalloides* consumption. Case 2: A 10-year-old boy consumed mushrooms in a meal and 12 hours later he developed severe diarrhoea, vomiting and became unconscious. He was treated with silibinin and N-acetylcysteine and received MARS prior to a successful liver transplant 6 days after ingestion. **Conclusion:** The severity of poisoning after mushroom ingestion varies depending on the amount ingested and the age of the affected person. The smaller the child, the more dangerous the situation. Unintentional ingestion of parts of a single mushroom can usually be managed with home observation, but without appropriate and immediate therapy *Amanita phalloides* can cause life-threatening intoxication. Deaths from *Amanita phalloides* are rare in children.

### 301. Herb intoxication: a folk medicine-induced anticholinergic syndrome

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**Objective:** Use of herbal medicine can result in poisoning but it can be difficult to identify, particularly where the patient or relatives vehemently deny ingestion of any toxic plant material. *Datura metel* was previously a popular herb used to treat bronchial asthma and chronic bronchitis; however, use can result in anticholinergic poisoning due to the presence of atropine and scopolamine. Anticholinergic poisoning causes mydriasis, flushing, dry skin, altered mental status and fever. We present a case of *Datura metel* poisoning which was difficult to diagnose. **Case report:** A 53-year-old male was brought to our emergency department because of altered mental status, disorientation and fever. Physical examination revealed reddish, dry skin and dilated pupils. Two hours previously, he had taken three types of decocted herbs, which included 110 g of honeysuckle flower, 40 g of guava leaf and 190 g of Nao Shen flower. The first two herbs are not toxic at the correct dosage, but information on Nao Shen flower was not available in any publication or article on the Internet or in books. His family were certain that no anticholinergic substance had been used. Initially, a benzodiazepine was prescribed for agitation but the symptoms did not improve. A total of 4 mg of physostigmine was then given but the patient remained stuporous. He was given more benzodiazepine and improved 24 hours after taking the herbs. One week later, a drug screen found the urine was positive for atropine and scopolamine. The herbs were examined by the College of Traditional Chinese Medicine and Nao Shen flower was thought to be *Datura metel*. **Conclusion:** Our patient presented with classic signs of anticholinergic toxicity, but no antidote was prescribed initially, because the physicians were reluctant to prescribe physostigmine where the usage of an anticholinergic substance was uncertain. In this case physostigmine was given as the patient remained unconscious which we believed resulted from the use of benzodiazepine or ingestion of an anticholinergic substance. The final diagnosis in this patient was anticholinergic poisoning. Physicians should prescribe physostigmine more promptly if there is a high index of suspicion of severe anticholinergic syndrome with seizures, arrhythmia or agitation and where there is no contraindication for physostigmine use.[1]

#### Reference

- [1] Burns MJ, Linden CH, Graudins A, et al. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. *Ann Emerg Med.* 2000;35:374–381.

### 302. Intoxications due to wild mushrooms collected by immigrants and asylum seekers in the Netherlands

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**Objective:** In the Netherlands collecting wild mushrooms for human consumption is not a general custom. Nevertheless, the Dutch National Poisons Information Center (DPIC) is regularly consulted about intoxications due to the consumption of self-gathered mushrooms. Our hypothesis is that immigrants are more often involved in wild mushroom intoxications when compared to native inhabitants. This hypothesis was tested by prospectively collecting all available demographical data of the patients. **Methods:** From January 2014 to 9 October 2015, a set of standardized demography related questions (including age, gender, and country of origin) was asked in all consultations concerning intoxications due to consumption of self-collected wild mushrooms. **Results:** During the study period, the DPIC was consulted 26 times concerning intoxications caused by wild mushrooms, ranging from 1 to 2 patients per incident. In total 33 patients were involved; 13 males and 20 females. Ages ranged from 2 to 78 years, with an average of 45 years. The nationality of 30 patients was known: 8 native Dutch (27%) and 22 non-Dutch (73%). The non-Dutch patients originated from Syria (5), China (3), Poland (3), Turkey (3), Germany (2), Slovakia (2), Russia (1), Thailand (1), Vietnam (1), and an unspecified Middle Eastern country (1). It is notable that 5 patients were staying in asylum seekers' centers at the time of ingestion. **Conclusion:** The majority of patients with an intoxication due to self-collected mushrooms in the Netherlands was of non-Dutch origin. Most patients came from countries in Eastern Europe, the Middle East or South East Asia, where gathering mushrooms for consumption is more common. With the recent arrival of more immigrants and asylum seekers in the Netherlands, the number of mushroom intoxications may increase in the future. Part of the problem seems to be a lack of awareness of the presence of very toxic mushrooms in the Netherlands, including *Amanita phalloides* (death cap). These concerns were communicated to the Dutch Central Agency for the Reception of Asylum Seekers (COA). This agency is currently warning asylum seekers about the toxicity of wild mushrooms in the Netherlands by means of spreading warning posters with pictograms. To what extent this may help prevent serious mushroom poisonings in the future will be followed-up.

### 303. Toxic courgette (zucchini) poisoning – cucurbitacin

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**Objective:** An enquiry to NPIS Edinburgh concerning a 79-year-old woman who ingested a bitter-tasting courgette and suffered from vomiting, diarrhoea and abdominal pain for the next 5 days prompted a review of UK National Poisons Information Service (NPIS) records for enquiries concerning members of the gourd family. **Methods:** Information was extracted from telephone

**Table 1.** Cases involving members of the gourd family reported to the NPIS.

Plant	Patients	Bitter taste	Exposure	Features
Courgette	Adults (2)		Skin contact (2)	Inflammation (1), rash (1)
	Adults (5), child (1)	Yes (5)	Ingestion	Ulcer on tongue (1) GI signs (4 including bloody diarrhoea 1) Asymptomatic (1)
Cucumber Gourd (5 ornamental, 5 bitter gourd)	Adult Adults (16)	Yes Yes (7)	Ingestion	Tremor GI (13) Burns to mouth / oesophagus (2) Haematemesis, renal failure and hyperkalaemia (1) Haemorrhage rectum (1) Asymptomatic (2)
Marrow	Adult			GI (bloody diarrhoea)
Melon	Child Adult		Ingestion of skin Seeds in soup	Asymptomatic Vomiting
Pumpkin	Adult		Leaves	Mild abdominal pain
	Adult			Diarrhoea, haemorrhage rectum
Squash	Adults (3)	Yes	Cooked	Abnormal sensation (2) GI signs (1)

enquiries received by the NPIS and recorded on the UK Poisons Information Database (UKPID) from 1 January 2008 to 31 August 2015. **Results:** Thirty-three records were retrieved concerning 32 incidents involving 31 adults and 3 children (Table 1). Enquiries concerning gourds (bitter or ornamental) occurred most commonly. Two cases involved skin contact with courgette leaves, the remainder were ingestions, generally involving cooked product. However, in some cases ornamental gourds were cooked and eaten and in one case an ornamental gourd was used as a container for tea. Drinks were also prepared using the vegetables. Gastrointestinal (GI) features were common (76.7% of ingestions), and included nausea, vomiting, diarrhoea and abdominal pain. Bleeding (in vomit or rectally) was mentioned in 4 cases. In 10 cases the patients were noted to report a bitter taste. **Conclusion:** Exposure to bitter-tasting members of the gourd family may result in gastrointestinal upset with bleeding which may last several days. While no actual confirmation of the toxin is available, many of the cases are similar to those reported in cucurbitacin poisoning.[1] As a result of mutation edible members of the gourd family e.g. courgette, cucumbers, melon, pumpkin, etc. occasionally produce toxic cucurbitacins which are more commonly found in wild variants. This results in very bitter tasting fruit that may cause poisoning.

## Reference

- [1] Ho CH, Ho MG, Ho SP, et al. Bitter bottle gourd (*Lagenaria siceraria*) toxicity. *J Emerg Med.* 2014;46:772–775.

## 304. Revenge of the zucchinis – is this the result of climate change?

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**Objective:** Colitis with bloody diarrhoea after consumption of zucchini (*Cucurbita pepo*) has been reported sporadically. Usually, the responsible toxins, cucurbitacins, are not detected in cultivated fruits, but some fruits spontaneously generate them. During 2002–2015 Poison Information Centre (PIC) Munich registered 81 symptomatic cases with clusters in the years 2003 and 2015, both with hot, dry summers. **Case reports:** Case 1: Three hours after a meal of vegetable stew with one green, bitter-tasting zucchini, home grown from commercial seeds, a 78-year-old man with pre-existing diabetes developed abdominal cramps and bloody diarrhoea. On admission one day later he had persistent bloody diarrhoea, hyperglycemia, acute renal failure and altered mental status. Despite aggressive supportive, antihyperglycemic and antibiotic care on day 3 he developed peritonitis from necrotizing colitis with septic multiorgan failure and cardiac arrest, necessitating cardiopulmonary resuscitation, mechanical ventilation, hemodialysis and emergency colectomy. He was extubated on day 10, re-intubated on day 13 and died from pneumonia on day 21. Case 2: A 78 year-old-woman ate a stew with one home grown, yellow, bitter-tasting zucchini. She was admitted to the hospital with abdominal cramps and initially bloody diarrhoea. With supportive care, diarrhoea persisted until day 3, but was no longer bloody. Case 3: A 78-year-old male, husband of case 2, with pre-existing diabetes, chronic renal insufficiency (creatinine 2.5 mg/dL) and arteriosclerosis, experienced spastic, bloody diarrhoea 1 hour after the meal. This resolved after 4 days of supportive care in hospital. Body fluids for toxicological analysis were collected 32 hours (case 1) and 14 hours after ingestion (cases 2 and 3). Cucurbitacin-E-glucoside (CucE-G) and aglycon cucurbitacin-E (CucE) were measured by high performance liquid chromatography-mass spectrometry (HPLC-MS) after alkaline liquid-liquid extraction. Results (ng/mL) were CucE-G/CucE, serum case 1: 2.0/not detected (ND); case 2: 0.6/ND; case 3: 0.5/ND; urine case 1: 4.6/8.8, case 2: 0.6/2.5, case 3: 1.5/1.7, gastric juice case 1: 91.0/29.0; stool case 3: 0.7/10.6. Fruits harvested from the plant responsible for case 1 were investigated by liquid chromatography/time-of-flight/mass spectrometry (LC/TOF/MS) after acetonitrile extraction (mg/kg): CucE-G 1139; CucE 8.28; total cucurbitacin 1580. **Conclusion:** We found a correlation between summer temperatures, rainfall and PIC calls concerning symptoms after zucchini meals. Bitter-tasting zucchini can cause life-threatening colitis. The responsible toxins can be detected in body fluids and fruits. During hot, dry summers the incidence of PIC calls with zucchini-related symptoms may increase. Authorities should be alerted by PIC when such cases occur.

## 305. Plant poisonings in the Slovak Republic from 2005–2014

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**Objective:** During a 10-year period the National Toxicological Information Centre (NTIC) in Bratislava received 36,138 enquiries from all over Slovakia. Plant exposures represent 4.5% of all cases collected by NTIC. We sought to characterise these enquiries in more detail. **Methods:** A retrospective analysis of all telephone calls to the NTIC between 2005 and 2014. **Results:** During the 10-year period 1619 plant exposures were reported to the Slovak PIC. Adults made up 16% and children 84% of all the reported cases (80% of children were less than 5 years old). Accidental exposures occurred in 93.7% of cases, abuse 6% and suicide attempts 0.3%. The most common route of exposure was ingestion (97%). NTIC answered most calls during the autumn (36.5%) and summer 32% with 18% of enquiries in spring and 13.5% in winter. The most frequently ingested plants were: *Datura stramonium* (6.5%), *Taxus baccata* (6%), *Zamioculcas zamiifolia* (4%), *Viscum album*, *Atropa belladonna*, *Ficus* plants and *Sambucus ebulus*. In 77% of patients no symptoms were reported, in 19% minor symptoms occurred and in 3.5% only moderate symptoms were reported. Eight patients developed severe symptoms. In seven of them the symptoms were associated with plants containing atropine-like alkaloids. One patient developed severe cardiovascular symptoms after ingestion of a potentially lethal dose of *Taxus baccata* needles. One person died after accidental ingestion of *Colchicum autumnale*. **Conclusion:** Most plant ingestions in children were not associated with the development of symptoms because only a small amount of plants was ingested. Poisoning due to mistaken identity may also occur; accidental poisoning by *Colchicum autumnale* occurred when it was mistaken for wild plants such as *Allium ursinum*.

### 306. Reversible neurotoxicity, gastrointestinal and visual disturbances after consumption of the onion earthball, *Scleroderma cepa* Pers: a case report

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**Objective:** Earthballs are a family of puffball-like mushrooms, generally estimated as being moderately toxic causing merely gastrointestinal disturbances. Medical literature about poisoning is sparse. However, some field guides and one mycological case report describe reversible neurological symptoms and visual disturbances (blurred vision, allochromasia and blindness) after consumption of *Scleroderma verrucosum* and *Scleroderma citrinum*. We report a case of toxicity after ingestion of *Scleroderma cepa*. **Case report:** A 42-year-old male and a friend ate a meal of self-collected *Scleroderma cepa*. The mushrooms were adequately fried for 20 minutes. He ate 3–4 and his friend ate one mushroom. They drank no alcohol. After 20 minutes he developed dizziness and 40 minutes after intake both had nausea. The friend recovered rapidly but the patient started to vomit, felt a sudden, depressive change of mood accompanied by visual hallucinations, double vision and blurred vision whereupon he sought help. After 3–4 hours his vision deteriorated to achromatopsia, which

resolved spontaneously over the next hours. Nausea and vomiting persisted until the next day as well as minor visual impairment and subsided with no specific measures within 48 hours after intake. However, he felt generally weak for the following two days before recovering completely. A specimen of the collected mushroom was retrieved and was identified macroscopically as well as by microscopy as *Scleroderma cepa*. **Conclusion:** To our knowledge this is the first report of a poisoning with *Scleroderma cepa*. Symptoms were gastrointestinal, neurological, mental and visual disorders including depression, hallucinations and achromatopsia. The course was benign with spontaneous recovery within four days. Similar toxidromes have been reported after ingestion of other *Scleroderma* species. Therapy is supportive. Some constituents of the related species *S. citrinum* have been identified and were investigated for their bioactive properties. A lanostane-type triterpenoid showed antiviral activity; *in vitro* vulpinic derivatives had anti-mycobacterial and cytostatic properties.[1] However, the nature of the neurotoxin causing this unique course of mushroom poisoning is still unknown.

### Reference

- [1] Kanokmedhakul S, Kanokmedhakul K, Prajuabsuk T, et al. A bioactive triterpenoid and vulpinic acid derivatives from the mushroom *Scleroderma citrinum*. *Planta Med.* 2003;69:568–571.

### 308. Paralytic ileus and anticholinergic toxicity after ingestion of incorrectly prepared lupin seeds

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**Objective:** Lupin is the common name for nearly 500 species of legumes. Some form part of the traditional Mediterranean diet. *Lupinus angustifolius* and *L. albus* are the main species cultivated for consumption and ground to make lupin flour. Lupin seeds are divided into sweet and bitter varieties. Bitter varieties contain a higher concentration of anticholinergic alkaloids. A debittering process including soaking and boiling over several days reduces alkaloid content. We report a case of severe paralytic ileus and anticholinergic toxicity after ingestion of under-prepared lupin seeds. **Case report:** A 56-year-old male with diabetes and hypertension, presented to the emergency department (ED) with generalised weakness, vomiting and abdominal pain. His symptoms started the day before presentation after consuming a fistful of lupin beans. Soon after ingestion he felt unwell, posturally dizzy, with dry mouth and difficulty urinating, worsening overnight with generalised colicky abdominal pain, distension and obstipation. There were no visual disturbances, confusion or delirium. A notable sign was an extremely dry mouth. In the ED he was hypotensive (82/50 mmHg), heart rate 86 beats/min, temperature 36.8 °C, oxygen saturation 97% (room air) with normal mental state. The abdomen was distended with absent bowel sounds. Left iliac fossa tenderness and urinary retention were noted. Twelve-lead ECG, full blood count, liver function tests and serum lipase were normal. Abdominal CT revealed dilated proximal and mid-small bowel without evidence of mechanical obstruction. He was fluid resuscitated but remained moderately hypotensive for several hours. He was admitted for observation under the surgical team. Symptoms slowly improved over 24 hours. Subsequently, he revealed that he soaked the lupin beans for three days rather than the usual five before boiling. When ingested he noted an

unusually bitter taste. The patient's wife also ingested a smaller amount of seeds and developed dizziness and dry mouth, but did not seek medical attention. **Conclusion:** This patient did not follow the process usually performed by his spouse for removal of the alkaloids from the seeds. Previous reports of lupin toxicity describe persistent anticholinergic symptoms and delirium after ingesting underprepared beans and flour,[1] however, this is the first case describing severe paralytic ileus following bean ingestion. Under-preparation of traditional foods by inexperienced hands can result in significant poisoning. This may become more common as new fads emerge touting the next "super-food".

## Reference

- [1] Litkey J, Dailey MW. Anticholinergic toxicity associated with the ingestion of lupini beans. *Am J Emerg Med.* 2007;25:215–217.

## 309. A case of severe cardiac arrhythmias after aconite poisoning with botanical and analytical confirmation

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**Objective:** The dangerous reputation of aconite (or monkshood) is rooted in the collective psyche, where this plant is said to be the most toxic of Europe. Aconitine is responsible for a toxidrome of neurological and cardiac symptoms.[1] This case report describes a voluntary poisoning from aconite root with botanical and analytical confirmation. **Case report:** A 55-year-old man presented with drowsiness and paraesthesia 2 hours following suicidal ingestion of aconite root (approximately 20 g) grown in his garden. During transport to an intensive care unit (ICU), his condition rapidly deteriorated with hemodynamic instability, polypnoea and vomiting. He had acute respiratory failure and a ventricular tachycardia required intubation/ventilation and two external electric shocks followed by cardiac massage, respectively. He also received 50 g of activated charcoal, 1000 ml of saline, 4 g of magnesium sulfate, 300 mg amiodarone and was intubated and infused with 0.6 µg/kg/min of norepinephrine. At the ICU he presented with tachycardia (110–160 beats/min) with chaotic rhythm (QTc 490 ms, QRS 0.11 s). A cardiac pacing catheter were placed and he was given esmolol to slow the heart to 60 bpm. Admission blood gases showed a compensated respiratory alkalosis (pH 7.43, pCO<sub>2</sub> 33 mmHg, bicarbonate 21.2 mmol/L). Evolution was favourable and treatment was stopped on day 3. Urinary infection and aspiration pneumonia were both treated with antibiotics. The plant was identified by our local botanical expert as *Aconitum* species from a photograph. Plasma and urine concentrations of aconitine measured by liquid chromatography coupled to high-resolution tandem mass spectrometry were 1.95 ng/mL and 2412.5 ng/mL, respectively. **Conclusion:** This case had a favorable outcome despite a lethal amount of aconite ingested, thanks to the rapid implementation of supportive methods and cardiac resuscitation.[2] Aconitine is the major and the most arrhythmogenic alkaloid in aconite.[1] This case illustrates the collaboration between experts in botany, analytical toxicology and clinicians to identify the toxic agent involved.

## References

- [1] Chan TY. Aconite poisoning. *Clin Toxicol (Phila).* 2009;47:279–285.  
[2] Gottignies P, El Hor T, Tameze JK, et al. Successful treatment of monkshood (aconite napel) poisoning with magnesium sulfate. *Am J Emerg Med.* 2009; 27:755.e1–4.

## 310. Fatal colchicine poisoning after accidental ingestion of autumn crocus (*Colchicum autumnale*)

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**Objective:** Ingestion of *Colchicum autumnale* (autumn crocus) may cause severe poisoning with lethal outcome. **Case report:** A 48-year-old man was admitted in the Poisoning Treatment Center 12 hours after he had accidentally cooked, and eaten a *Colchicum autumnale* bulb, what he had thought was an onion. Four hours later he had developed gastrointestinal pain, nausea, vomiting, and abundant diarrhea. On admission he was conscious with pale dry skin, heart rate 88 beats/min and arterial pressure 150/90 mmHg. Laboratory test results on the intensive care unit admission were as follows: hemoglobin 183 g/L (normal range 135–160 g/L), erythrocytes  $5.84 \times 10^{12}/L$ , leukocytes  $7.39 \times 10^9/L$  (normal range  $4.2\text{--}0.7 \times 10^9/L$ ), haematocrit 50.9 g/L, platelets  $86.6 \times 10^9/L$  (normal range  $150\text{--}400 \times 10^9/L$ ), urea 7.20 mmol/L (normal range 2.5–8.3 mmol/L), serum creatinine 129.6 µmol/L (normal range 44–106 µmol/L), aspartate aminotransferase at 276.0 IU/L (normal range 13–40 U/L) and alanine aminotransferase at 88.6 U/L (normal range: 7–40 U/L). Hemostasis parameters were as follows: prothrombin time 48% (normal >70%), International Normalized Ratio 1.57 (normal 0.7–1.2), Electrocardiogram (ECG) showed sinus heart rate and moderate alteration of myocardium. Other system examinations were unremarkable. Gastric lavage, activated charcoal, IV sodium chloride, dextrose, saline solutions, forced diuresis and symptomatic treatment were performed. During 2–3 days after hospitalization gastrointestinal symptoms disappeared, he improved and status was stable. By the end of the 4th day after poisoning he complained of shortness of breath, dyspnea with respiratory rate 30–32 breaths/min. Chest X-ray showed congestion in the lungs and left heart enlargement. Heart rate was 118 beats/min, arterial pressure 175/90 mmHg and temperature 38.0 °C. He was sedated, intubated, and mechanically ventilated due to respiratory distress. The clinical course was marked by pancytopenia: hemoglobin, platelet, and leukocyte count nadir were 101 g/L,  $2.0 \times 10^9/L$ , and  $0.2 \times 10^9/L$ , respectively. He had diffuse bleeding at puncture points, hemoptysis and hematuria requiring blood product transfusion (4 doses platelet concentrates, a total 400 mL after which the platelet count increased to  $21.0 \times 10^9/L$ , and 2 doses fresh frozen plasma, total 500 ml) and treatment with tranexamic acid. At that time major hemodynamic instability developed as a manifestation of cardiogenic shock requiring continuous infusion of high doses of dobutamine (up to 10 mcg/kg/min). He rapidly deteriorated and died at the end of the fourth day after ingestion. **Conclusion:** *Colchicum autumnale* contains colchicine and is extremely toxic. Ingestion of one bulb was lethal in this case.

### 311. Fatal common yew ingestion with serum taxine confirmation

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**Objective:** Common yew (*Taxus baccata*, European yew or English yew), is a decorative shrub commonly found in North America. Taxine alkaloids have been identified as the most likely cause of toxicity associated with yew ingestion.[1] Significant yew ingestions result in ventricular dysrhythmias, hypotension and often cardiac arrest resistant to standard therapies.[2] We present a case of fatal yew ingestion with serum confirmation. **Case report:** A 22-year-old female was brought in by ambulance from a nearby botanical garden in cardiac arrest. The patient had just walked out of the botanical garden exhibit when she had a witnessed generalized tonic clonic seizure. Bystanders found the patient pulseless and apneic, and resuscitative efforts were initiated. Emergency Medical Services arrived and found the patient in ventricular tachycardia, and restored pulses after cardioversion, 300 mg amiodarone, and 6 mg epinephrine. On arrival to the Emergency Department (ED), the patient had blood pressure 65/40 mmHg, heart rate 32/min, respiratory rate 17/min, pulse oximetry 65% with bag valve mask and the patient was immediately intubated. She was noted to be in a wide complex rhythm and persistently hypotensive. She was treated with intravenous fluids, atropine, epinephrine, calcium chloride, sodium bicarbonate, glucagon, and intravenous lipid emulsion without improvement. The patient's initial venous blood gas prior to intubation was pH 7.20, PCO<sub>2</sub> 70 mmHg, PO<sub>2</sub> 21 mm Hg, and a bicarbonate 26 mEq/L. Her initial chemistry panel was remarkable for a potassium of 2.5 mEq/L, bicarbonate of 18 mEq/L, glucose of 219 mg/dL and an anion gap of 17 mEq/L. After a discussion with the Poison Control Center, the patient was treated with digoxin Fab fragments. Despite supportive care measures and pressor support with intravenous epinephrine the patient expired approximately 2 hours after her arrival in the ED. The patient's antemortem blood showed detectable concentrations of taxine A and B, as well as 3,5-dimethoxyphenol, another compound found in yew. **Conclusion:** Significant yew ingestions may result in ventricular dysrhythmias and cardiac arrest that is resistant to standard therapies. Early and aggressive gastrointestinal decontamination should be considered as well as extracorporeal life support measures.

#### References

- [1] Wilson CR, Sauer JM, Hooser SB. Taxines: a review of the mechanism and toxicity of yew (*Taxus* spp.) alkaloids. *Toxicol.* 2001;39:175–185.
- [2] Willaert W, Claessens P, Vankelecom B, et al. Intoxication with *Taxus baccata*: cardiac arrhythmias following yew leaves ingestion. *Pacing Clin Electrophysiol.* 2002;25:511–512.

### 312. Amatoxin poisoning during pregnancy: a case report and review of the literature

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**Table 1.** Summary of cases of amatoxin exposure in pregnancy reported in the literature.

Poisoning in gestational week	Outcome	Author (year)
6	Induced abortion, medical reasons	Timar (1997)
6	Spontaneous abortion	Trabulus (2011)
7	Healthy child	Trabulus (2011)
8	Minor abnormalities, full term	Timar (1997)
9	Induced abortion, precautionary measure	Kaufmann (1978)
11	Healthy child, full term	Boyer (2001)
20	Healthy child, full term	Timar (1997)
20	Healthy child, gestational week 36	Wu (2004)
22	Healthy child, full term	Dolfi (1994)
23	Healthy child, full term	Nagy (1994)
24	Healthy child	Jaros (1996)
28	Fetal alcoholic syndrome, gestational week 36	Timar (1997)
28	Healthy child, full term	Schleufe (2003)
28	Healthy child, full term	Our case (2014)
8 months	Healthy child, full term	Belliardo (1983)
39	Healthy child, full term	Wacker (2009)
Unknown	Mother and fetus died	Varshochi (2007)
Unknown	Mother and fetus died	Varshochi (2007)

**Objective:** Little is known about amatoxin poisoning during pregnancy. Opinions differ on whether amatoxins pass the placenta, but more recent publications suggest that it is not the case. We present a case report and a literature review to further elucidate this subject. **Case report:** A 31-year-old Syrian woman, in gestational week 28, living in refugee accommodation had onion and mushroom soup for dinner. After 10–12 hours she developed nausea, vomiting, gastric pain and diarrhea. The mushroom was identified as *Amanita virosa*. She was treated for three days according to the Swedish protocol with N-acetylcysteine, silibinin and activated charcoal. The urinary amatoxin concentration approximately 20 hours after the meal was high, >100 µg/L (reference <2), but she did not develop liver failure (liver enzymes remained normal). Three months later she gave birth to a healthy child at full term. (This case was briefly been mentioned in *Clinical Toxicology* 2015; 53:342). **Results:** In total 17 additional cases were identified (Table 1). **Conclusion:** Altogether the outcome of the included cases strongly indicates that amatoxins do not pass the placental barrier, even though the information about the cases in the first trimester is limited. In the future, sampling from the amniotic fluid would be valuable and could possibly establish this fact. Amatoxin poisoning does not seem to affect the length of the pregnancy and the treatment used in the Swedish protocol for amatoxin poisoning does not involve any risks for the fetus. Therefore, in amatoxin poisoning in pregnant women focus should be optimal treatment of the mother.

### 313. Plant names matter when recording poisoning cases and retrieving information: Kew's Plant Names Services for Health provides solutions

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**Objective:** Appropriate treatment and advice in poisoning cases from plants or plant-based medicines relies on using

unambiguous names for those plants. Non-scientific names (e.g. laurel, oleander or fang ji) are often ambiguous, yet are frequently the only name available in case reports. Retrieval of all past cases or references relating to a particular plant depends on knowing all possible names used for that plant, but where can you find this information? Scientific names are the only reliable means for information retrieval and exchange, yet appropriate use of scientific nomenclature can be challenging. Kew's Medicinal Plant Names Services (MPNS) initiative, funded by the Wellcome Trust 2012–2016, provides a suite of services to increase the relevance and accessibility of Kew's plant name resources to the health community. Central to this has been the mapping of all names used in key medicinal plant references, such as pharmacopoeias, to Kew's taxonomy and nomenclature. MPNS has achieved recognition amongst health regulators globally, with increasing demand for our "validation" and "controlled vocabulary" services. An MPNS vocabulary is part of the new ISO data standard for identification of medicinal products (IDMP). Kew's Plant Names Services now seek to reach new audiences, to cover plants relevant to food supplements and toxicity, and to meet the needs of poisons information centres and clinics. **Methods:** A user group, comprising representatives from poison centres, food regulation, research and manufacturing, were questioned on a one-to-one basis, and through workshops, to determine priorities for appropriate solutions. Supplementary views will be sought as development proceeds. **Results:** Including non-scientific names in our controlled vocabularies, and modifications to the portal ([www.kew.org/mpns](http://www.kew.org/mpns)) to enable links from other online resources, have been identified as priorities for enhanced services. The collection and display of additional data of most use to these audiences includes the class and name of reported toxins, and animal subject. Funding applications have been submitted for this next phase, and we seek new partners in this enterprise. **Conclusion:** The MPNS resource covers 13,500 plants of known medicinal use and contains over 80,000 names used in the medicinal literature and 240,000 names from Kew's resources. MPNS is already useful to poison and pharmacovigilance centres handling enquiries about plant-based medicines. By extending MPNS to include plant food supplements (including adverse effects) and toxic plants (allergens, human and animal poisoning), it will facilitate the provision of more comprehensive advice regarding cases of suspected poisoning.

### 314. *Diospyros rhodocalyx* (Tako-Na), a Thai folk medicine, as a cause of hypokalemia, proximal muscle weakness and hypertension

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**Objective:** *Diospyros rhodocalyx* (Tako-Na) is a Thai folk medicine purported to promote longevity, treat impotence, etc. We present patients with hypokalemia, weakness and hypertension after consuming Tako-Na tea. We searched Medline and Google, but could find no reports on such adverse effects from this plant. **Case series:** Case 1: A 60-year-old man was brought in 9 hours after drinking 2 glasses of Tako-Na tea. One handful of Tako-Na bark was boiled in a liter of water to make the tea. He had vomiting and watery diarrhea 6 hours after ingesting the tea. He took no medications and had no prior history of hypertension. The only

remarkable vital sign was blood pressure (BP) 167/90 mmHg. Physical examination revealed generalized proximal muscle weakness (grade 3). Laboratory findings were sodium 140 mmol/L, potassium 2.7 mmol/L, bicarbonate 24, and trans-tubular potassium gradient (TTKG) 5.6. Initial electrocardiogram (ECG) showed a QTc of 597 ms which was shortened after potassium supplementation. He was discharged home the next day with a BP 140/90 mmHg and potassium of 4.2 mmol/L. Case 2: A 72-year-old man, friend of case 1, also drank Tako-Na tea from the same pot at the same time as case 1 but only ingested one glass. He also had vomiting and watery diarrhea 6 hours later. He took no medications despite past history of hypertension (baseline systolic BP 140–160). At presentation, his blood pressure was 230/70 mmHg. He also had proximal muscle weakness. Laboratory findings were sodium 144 mmol/L, potassium 3.3 mmol/L, bicarbonate 24, TTKG 7.37, and normal thyroid function tests. His initial ECG showed bigeminy which resolved after potassium supplementation. He was also discharged the next day with a BP 148/70 mmHg and potassium 4.2 mmol/L. Cases 3–7: These were patients reported to the poison center and their potassium concentrations were as following: 1.4, 1.4, 3.3, 1.3 and 1.2 mmol/L, respectively. Three of them were intubated. Case 3 with a potassium concentration of 1.4 mmol/L died. **Conclusion:** Tako-Na contains betulin, betulinic acid, taraxerone, lupeol, and lupenone. Their structures are similar to glycyrrhetic acid, the active metabolite of glycyrrhizic acid found in licorice which is well known to cause pseudoaldosteronism (hypokalemia-causing weakness and water and sodium retention-causing hypertension). Glycyrrhetic acid is 200–1000 times more potent than glycyrrhizic acid in inhibiting 11-beta-hydroxysteroid dehydrogenase, and causes pseudoaldosteronism. We hypothesize that the compounds in Tako-Na act in the same way as glycyrrhetic acid in producing pseudoaldosteronism.

### 315. Reasoning by analogy might not always be reasonable: failure of ricinine to predict severity of ricin poisoning in a castor bean ingestion

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**Objective:** To describe the risks of predicting ricin toxicity by detecting ricinine in castor bean ingestion. **Case report:** A 22-year-old male was admitted after intentionally ingesting 10 seeds of *Ricinus communis* (castor bean). He masticated the seeds thoroughly about 10 hours before being admitted, calling the ambulance after experiencing vomiting and abdominal cramps with diarrhoea. He presented with tachycardia and mild abdominal discomfort, but had no further gastrointestinal or other clinical signs in the following days; laboratory findings remained normal for electrolytes, kidney and liver function. There was a 2- to 3-fold increase in free haemoglobin (max 163 mg/L) as the only marker indicating haemolysis; erythrocytes and haemoglobin remained normal. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed to detect ricinine as a surrogate for ricin,<sup>[1]</sup> showing markedly elevated concentrations in serum and urine 10 hours after ingestion (67.9 ng/mL and 232 ng/mL, respectively). He was discharged after 7 days without any sign of clinical impairment. **Conclusion:** Castor beans contain both ricinine and ricin, and as detection of ricin can be difficult the detection of the ricinine is used as a surrogate for the presence – and toxicity – of ricin. Case reports showing fatal outcomes with similarly elevated

concentrations for ricinine as in our case have been published,[2] but others have also shown,[3] as in our case shows, that this analogy may be misleading. Bearing in mind the variety of cultivars of *Ricinus* seeds one may speculate that the ratio of ricin to ricinine in the seeds was low in our case and therefore overestimated the expected ricin. If this was true, a hypothetical contrary ratio could lead to an even more troublesome underestimation of toxicity. The prediction of ricin toxicity by measuring ricinine concentrations might be misleading. A possible confounder could be the variation of the concentrations of the two substances in castor beans.

## References

- [1] Worbs S, Köhler K, Pauly D, et al. *Ricinus communis* intoxications in human and veterinary medicine – a summary of real cases. *Toxins* (Basel). 2011;3:1332–1372.
- [2] Røen BT, Opstad AM, Haavind A, et al. Serial ricinine levels in serum and urine after ricin intoxication. *J Anal Toxicol*. 2013;37:313–317.
- [3] Hamelin El, Johnson RC, Osterloh JD, et al. Evaluation of ricinine, a ricin biomarker, from a non-lethal castor bean ingestion. *J Anal Toxicol*. 2012;36:660–662.

## 316. Lessons to learn from fatal ingestion of *Prunus laurocerasus* leaves in a goat

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**Objective:** *Prunus laurocerasus* (cherry laurel) contains cyanogenic glycosides and, particularly in the form of well chewed leaves, is toxic to horses, cattle, goats, sheep, swine, dogs, cats, hares, rabbits, rodents (guinea pigs, hamsters) and birds. Ruminants are at particular risk due to the repeated chewing process and because the cyanogenic glycosides are split in the rumen by the action of microbial enzymes, resulting in an accelerated release of cyanide ions, which are able to penetrate lipid membranes. Cyanide ions bind to the central iron (III) ion in the mitochondrial respiratory chain with higher affinity than oxygen. Oxygen binding in the blood is inhibited, resulting in inhibition of the respiratory chain, internal asphyxia and multiple organ failure. The ingestion of major amounts by children or adults is rather improbable because the plant has an unpleasant taste, so that recent human toxicity assessments resulted in a "mild to moderate" rating only. We report a fatal veterinary case. **Case report:** A Thuringian forest goat had eaten about 1 kg of cherry laurel leaves. Subsequently, the animal developed gastrointestinal symptoms and apathy. On hospital arrival, the animal was found to be somnolent, with acral coldness, pale conjunctivae and a pronounced abdominal breathing with highly pronounced moist rales over the lungs. Laboratory findings included severe leukocytosis accompanied by a left shift, mild anaemia and thrombocytosis, hyperglycaemia, hypomagnesaemia, considerable increase in serum urea concentrations and elevated creatine kinase concentrations. Since the history of ingestion was unknown the animal was treated symptomatically and died on the third day after ingestion. The post-mortem examination found the rumen, reticulum and omasum to be filled with large quantities of fibrous matter consisting of poorly masticated leaves, later

identified as cherry laurel. Other findings included severe acute alveolar lung oedema, mild serofibrinous pleuritis and diffuse catarrhal enteritis. **Conclusion:** Regarding the toxic risk of cherry laurel ingestion in humans, the rare animal example has demonstrated the most important factors for the toxins to become released: 1) large amount, 2) intensive and repeated chewing as in ruminants and 3) specific rumenal releasing enzymes. This very rare worst case scenario could lead to fatal poisoning from the inherent cyanogenic glycosides. The existing chemical risk assessment is always based on complete substance release. Hence, the question arises as to whether such simple (inherent) risk assessment can indeed reflect reality.

## 317. Thai eggplant ingestion resulting in anticholinergic poisoning and ECG abnormalities

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**Objective:** To present a case of anticholinergic toxicity from "Thai eggplant" ingestion, and highlight the toxicity of glycoalkaloids in the *Solanum* genus. **Case report:** A 73-year-old Thai female with a history of hypertension was brought to the emergency department (ED) with confusion and inability to speak. The patient's family reported that she was eating a meal around 6 pm, felt tongue discomfort and took one loratadine tablet for a presumed allergic reaction. In the ED her vital signs were: temperature 36.6 °C, heart rate 114 bpm, blood pressure 150/100 mmHg, respiratory rate 20/min and oxygen saturations 100%. Her physical exam was notable for dilated pupils, dry mucus membranes and tachycardia. She was not able to follow commands and phonated incomprehensibly. She had up-going Babinski's and moved all four extremities spontaneously equally. Laboratory tests were unremarkable (basic metabolic panel, complete blood count, venous blood gas, liver function tests, and coagulation panel). The electrocardiogram (ECG) showed sinus tachycardia and a terminal right axis deviation in aVR. Chest X-ray and head computerised tomography (CT) scan were unremarkable. The patient's family further revealed that the meal had included uncooked "Thai eggplant" obtained from a neighbor's garden. A photo of the ingested plant was confirmed by a botanist working with the local Poison Control Center to be of the Solanaceae family: *Solanum melongena*. Although physostigmine was recommended given its effectiveness in anticholinergic poisoning,[1] it was withheld initially due to the patient's terminal right axis deviation and select case reports showing adverse cardiac effects, including asystole in patients with sodium channel blockade, with physostigmine use.[2,3] Her mental status vastly improved on day 3 and she was discharged home on hospital day 4. This is the first reported case of *Solanum melongena* poisoning in the US. **Conclusion:** Clinicians should identify and treat anticholinergic poisoning after *Solanum melongena* ingestion. It is important to educate the community regarding the potential for anticholinergic toxicity when ingesting this plant uncooked. Antidotal therapy with physostigmine should be considered, unless there is ECG evidence of concomitant sodium channel blockade.



## References

- [1] Burns M, Linden CH, Graudins A, et al. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. *Ann Emerg Med.* 2000;35:374–381.
- [2] Pentel P, Peterson CD. Asystole complicating physostigmine treatment of tricyclic antidepressant overdose. *Ann Emerg Med.* 1980;9:588–590.
- [3] Shannon M. Toxicology reviews: physostigmine. *Pediatr Emerg Care.* 1998;14:224–226.

## 318. Prolonged cardiotoxicity after significant ingestion of *Aconitum napellus* root

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**Objective:** Aconitine from *Aconitum napellus* (Family Ranunculaceae) is a toxic secondary plant compound. All parts of the plant contain toxic diterpene alkaloids, including aconitine. The lethal dose of aconitine is 3–6 mg for an adult, and as the seeds and roots may contain up to 2% alkaloid, a few grams of the plant is dangerous. Though plant extracts are well-known ingredients in folk medicines, *A. napellus* is not a permitted ingredient in medicines approved by the European Medicines Agency. **Case report:** A 76-year-old woman known to have periods of depression ingested a significant but unknown amount of *A. napellus* root in a suicide attempt. She peeled and sliced the root as uncooked garnish for her dinner of meatballs. Approximately 14 hours later she was found by her neighbour as she had fallen on the street wearing only thin clothes. Her symptoms included intense diarrhea, mouth itching, tingling in the fingers, arms and face, pain and vertigo; pre-hospital symptoms included muscular weakness in the hands. She had a normal temperature on arrival (37.2 °C). Pre-hospital electrocardiogram (ECG) showed fluctuating narrow and broadening complexes. Shortly after arrival she developed increasing numbers of extrasystoles and abnormal ECG with prolonged QTc (531 ms), ST elevation, QRS 108 ms, left-axis deviation (–57°), accelerated nodal rhythm with premature ventricular complexes. Blood pressure 180/80 mmHg, mean arterial pressure (MAP) 105 mmHg, heart rate approximately 85 beats/min, myoglobin >20,000 mcg/L, creatine kinase >20,000 U/L, ALT 95 U/L and creatinine 204 µmol/L. Her clinical status and laboratory values deteriorated further during the following 12 hours in the intensive care unit (ICU) with extrasystoles, QT prolongation, elevated magnesium (1.33 mmol/L) and rhabdomyolysis. Treatment included oral activated charcoal (100 g), forced diuresis (4000 mL/day) using furosemide and crystalloids, and nitroglycerin infusion to maintain blood pressure 150/80 mmHg and MAP 80 mmHg. After 2 days of ICU care the patient improved, except for nephrotoxicity caused by rhabdomyolysis, and was transferred to somatic and psychiatric care for further treatment. **Conclusion:** The patient survived a significant ingestion of *A. napellus*, characterised with classic symptoms of severe poisoning [1,2] but with prolonged cardiotoxicity. Intensive care and advanced symptomatic treatment provided the patient's survival.

## References

- [1] German Jørgensen JR, Andersen AE. [Fatal exposure to *Aconitum napellus*.] [Article in Danish] *Ugeskr Laeger.* 2013;175:1707–1708.
- [2] Plants – Aconitum. POISINDEX<sup>®</sup> System (electronic version). Truven health analytics, Greenwood Village, Colorado, USA; [cited 2015 Nov 21]. Available at: <http://www.micromedexsolutions.com/>

## 319. Expired antivenin: good efficacy in a severely envenomed cat bitten by *Sistrurus miliarius miliarius*

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**Objective:** Actual shelf-life of antivenins may be longer than their stated expiration date, but little is known about efficacy and safety of expired antivenin. There is only sparse literature on the *in vitro* efficacy of expired antivenin [1,2] and equally sparse reports on administration of the same in animals and humans.[3] We present a case of life-threateningly envenomation in a cat bitten by *Sistrurus miliarius miliarius* (Carolina pigmy rattlesnake) that benefited from antivenin that had expired eight and six years previously. **Case report:** A 7-year-old, 4.1 kg previously healthy female European shorthair cat belonging to a snake breeder was bitten on the snout by a juvenile *Sistrurus miliarius miliarius* and rapidly developed local edema. After 24 hours creatine kinase had risen to 25,403 U/L (range 77–355 U/L). Clotting assays (ROTEM<sup>®</sup> Thromboelastometry) detected a massive hypocoagulable state, characterized in an EXTEM test by a markedly prolonged clotting time (314 s; range 126–254 s), severely reduced maximum clot firmness (5 mm; range 40–78 mm) and unmeasurable clot formation time and  $\alpha$  angle (ranges 48–251 s and 53–80°, respectively). The owner had brought two vials of Antivipmyn<sup>®</sup> (Instituto Bioclon, Mexico) from his own stock, which had been stored correctly according to the manufacturer's instructions but had expired in 2007 and 2009. After the first vial (of 2009) was administered, coagulation started to improve with a clotting time of 99 s. Due to severe hyperfibrinolysis the second vial (of 2007) plus two doses of 20 mg/kg tranexamic acid were administered, after which coagulation returned to normal. Despite severe coagulopathy, the clinical condition was unremarkable, and the cat was discharged after 5 days in good health without further sequelae, except for a bald spot at the site of the bite. **Conclusion:** This case supports the assumption that commercial expired antivenin may be more robust than the expiry date would suggest and thus might be a therapeutic option in case of life-threatening envenomation, although further studies on the safety of expired antivenin are needed.

## References

- [1] O'Leary MA, Kornhauser RS, Hodgson WC, et al. An examination of the activity of expired and mistreated commercial Australian antivenoms. *Trans R Soc Trop Med Hyg.* 2009; 103:937–942.
- [2] Rentmeester L, Burton D, Fitzgerald R, et al. Immunoglobulin concentration & venom binding activity of expired snake antivenoms. *Clin Toxicol (Phila)* 2014;52:695.
- [3] Mannel R, Pudovka Gross OA, Gross GA. Coral snake antivenin's deadly deadline. *Toxicon.* 2012;60:225.

## 320. Epidemiology of scorpion stings in Morocco from 2005 to 2014

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**Objective:** Scorpion sting (SS) is the leading cause of poisoning in Morocco (30–50% of poisoning cases). In 2001 the Poison Control and Pharmacovigilance Centre of Morocco (CAPM) developed a national strategy for stings and scorpion envenomations,[1] centred around training of health personnel, information, education and communication to the public, improving management and finally monitoring and evaluation of the implementation of an information system [2] to monitor indicators of morbidity and mortality from SS. We present the epidemiology of SS from 2005 to 2014 and examine the indicators of fatal outcome. **Methods:** The collection of information was compiled by the provincial epidemiological moderator to study regional and national demographics, economics and evolving features of SS. **Results:** In total 270,100 cases were reported, of which 27% were children  $\leq 15$  years old. The sex ratio was 0.96. Simple sting without envenomation (Class I) accounted for 91.4% of cases. Cases admitted to a healthcare facility reflecting envenomation Class II and Class III accounted for 7.3% and 1.3% of cases, respectively, an overall envenomation rate of 8.6%. Cases referred to another health facility represented 9.7% of cases, hospitalized cases 5.3%, while 51.8% of patients required no treatment. There were 648 cases, of which 92.9% were children. The average fatality rate (deaths in patients with SS) was 0.24%, but this varied according to region and year (0.4% in 2005 to 0.1% in 2014). Moreover, the envenomation lethality rate (deaths in patients with class II and class III envenomation) was 2.8% overall (4.2% in 2005 compared to 1.2% in 2014); the lethality rate in children  $\leq 15$  years was 0.8% (1.18% in 2005 down to 0.5% in 2014). Overall the fatality rate in patients with Class III envenomation was 19.1% (37.4% in 2005 compared to 11.8% in 2014). **Conclusion:** Continuous improvement in monitoring of indicators of morbidity and mortality following SS allowed us to get closer to the objectives set. We note with satisfaction the streamlining of expenditures and lower fatality rates. Efforts are still needed to eradicate this scourge. For this, a widespread clinical audit of deaths by SS is necessary.

### References

- [1] Soulaymani Bencheikh R, Faraj Z, Semlali I, et al. [National strategy in the battle against scorpion stings and envenomations. Application and evaluation.] [Article in French] Bull Soc Pathol Exot. 2003;96:317–319.
- [2] Soulaymani-Bencheikh R, Semlali I, Ghani A, et al. Implantation et analyse d'un registre des piqûres de scorpion au Maroc. Santé Publique. 2004;16:487–498.

## 321. Spider bites in Southern France: 3 cases

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Table 1. Three spider bites managed during Summer 2015.

Case	Age (years)	Spider involved	Clinical presentation	Treatment	Evolution
1	77	<i>Latrodectus tredecimguttatus</i>	Latrodectism: Chest tightness, muscle cramps, tachycardia, local pain	Corticosteroids Calcium Benzodiazepine Painkillers	Healing without sequelae after 3 days of medical care
2	27	<i>Steatoda nobilis</i>	Steatodism: Headache, dysphagia, dyspnoea, hyperthermia, myalgia, facial swelling, local pain	Adrenaline Antihistamine	Healing without sequelae after 1 day of medical care
3	47	<i>Loxosceles rufescens</i>	Loxoscelism: Cutaneous necrosis, headache, hyperthermia, paresthesia, local pain	Antibiotics Corticosteroids Necrosectomy	Healing without sequelae after 7 days of medical care

**Objective:** Spider bites are frequent events in the summer in Southern France with around 50 evenomations managed by the Marseille Poison Centre every hot season. In Europe dangerous spider species are not numerous, but in the Mediterranean area several kinds of clinical picture are possible after a bite of a local spider species such as latrodectism, steatodism or loxoscelism. We report three cases managed during summer 2015 by the Marseille Poison Centre in order to illustrate the different aspects of araneism in Provence. **Cases series:** The 3 cases described in the table are typical of each kind of envenomation, with neuromuscular disturbances for latrodectism, low severity latrodectism-like syndrome for the steatodism and severe necrosis for the loxoscelism. **Conclusion:** Spider bites in the Mediterranean coast of France may result in severe envenomation. Medical management depends on the species of spider involved. Antivenoms for spider bite are not available in France where symptomatic treatments are only used for such events.

## 323. Viper envenomation in Greece: antivenom treatment in a case series (2014–2015) from the Greek Poison Information Center

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**Objective:** Venomous snakebites in Greece are caused only from species of the Viperidae family. *Vipera ammodytes* is responsible for the majority of envenomations and is found throughout the country.[1] Other snakes such as *Vipera xanthina*, *Vipera lebetina* and *Vipera berus* are located in specific geographic regions. The aim of this study was to describe the clinical course, indications and efficacy of antivenom treatment. **Methods:** A retrospective analysis of the PIC database regarding snakebites during the years 2014–2015 and case records concerning patients treated in Greek hospitals. **Results:** A total of 340 snakebite cases were reported during the study period. The patients were predominantly male (66%), mean age 35 years. Most snakebites happened in spring (18%) and summer months (56%) but there were also cases in February and November. Among 340 patients, 31% had dry bites

**Table 1.** Severity of envenomation of Viperidae bites.

Type of stings / symptoms	Mild	Moderate	Severe
Local	Swelling, erythema confined to bite site, minimal pain.	Progression of swelling, erythema beyond bite site, pain starts immediately after bite.	Rapidly progressive extensive swelling, erythema or ecchymosis involving the entire body part, immediate severe pain.
Systemic	No systemic signs or symptoms. No coagulation abnormalities or other laboratory abnormalities.	Non-life-threatening stings or symptoms. Mild coagulation abnormalities without significant bleeding.	Markedly severe signs or symptoms: hypotension, tachycardia, respiratory distress, coagulation abnormalities with bleeding, platelet count < 50,000/ $\mu$ L, increase in D-dimer, leukocytes, creatine kinase.

and 69% developed envenomation. In the 235 patients who developed envenomation the most common symptoms were local edema, erythema and pain, gastrointestinal signs (vomiting, diarrhea, abdominal pain), circulatory effects (hypotension, shock, electrocardiogram abnormalities), hematological changes (leukocytosis, hemolysis, coagulopathy) and allergic symptoms (urticaria, angioedema). The bites were categorized as mild in 40%, moderate in 35% and severe in 25% (Table 1). Administration of specific anti-Fab antivenom was required in 33.6% of patients and was indicated for all severe cases and in selected moderate cases. Antivenom treatment resulted in prompt clinical improvement. Adverse effects consisting of urticaria and serum sickness did not occur. There were no deaths. **Conclusion:** Antivenom therapy proved to be an effective and safe treatment in cases of severe envenomation. The occurrence of allergic side-effects was negligible with this type of antivenom.

## Reference

- [1] Frangides CY, Koulouras V, Kouni SN, et al. Snake venom poisoning in Greece. Experience with 147 cases. *Eur J Intern Med.* 2006;17:24–27.

## 324. Life-saving antivenom treatment after a Monocled Cobra bite in the Netherlands

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**Objective:** Since 2008, a National Serum Depot (NSD) has been operational in the Netherlands, guaranteeing rapid antivenom supply during medical emergencies. Antivenom from the NSD is (only) available after contact with the National Poisons Information Center (PIC). Here, we present a case of Monocled Cobra (*Naja kaouthia*) bite requiring antivenom. **Case report:** Ten

minutes after being bitten by a 1.5 metre long cobra, a 28-year-old amateur herpetologist was transported by ambulance to the University Medical Center Utrecht. On arrival at the Emergency Department (ED), he was nauseated with severe vomiting. Physical examination revealed bite marks on his left elbow. During the first 30 minutes, blood pressure increased from 150/85 to 195/102 mmHg, heart rate rose from 80 to 133 beats/min and respiration rate increased from 17 to 30 breaths/min, with decreasing saturation from 100% to 93% on room air. The patient had fixed dilated pupils, was combative and refused supportive respiratory measures. Thereafter, within minutes his overall clinical condition deteriorated, and he became unresponsive and cyanotic, requiring rapid sequence intubation and mechanical ventilation in the ED. Meanwhile, after contact with the PIC, 4 vials of Thai Red Cross Cobra antivenin were ordered from the NSD. At the Intensive Care Unit (ICU), antivenom was administered 2.75 hours after the bite. After antagonizing the remaining paralyzing effect of rocuronium-induced muscle relaxation (used during intubation) with sugammadex, the patient was able to trigger the ventilation machine. After cessation of the sedation, he woke up, and could communicate via squeezing his hand and shaking his head. As further neurological improvement was slow, additional antivenom (4 vials) was given 9.25 hours later. He was taken off the ventilator 5 hours later (17 hours post-bite). Within 24 hours after the bite, he could be discharged to the medium care unit, where mildly increased clotting times were noted and local effects appeared to be worsening. In addition to erythema, edema progressed to the hand and shoulder and a few small blisters appeared remote from the bite site. Pain was treated with opioids and antibiotics were started 24 hours later. He was discharged after 8 days. **Conclusion:** Antivenoms vary in price from <100 Euro to >1500 Euro per vial and often many vials are necessary to treat an envenomation effectively. Keeping rarely used antivenoms in stock is expensive. However, this case clearly shows that antivenom treatment is cost effective as mechanical ventilation duration was reduced by several days.

## 325. Efficacy of Crotalidae polyvalent immune Fab antivenom with delayed administration

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**Objective:** Demonstration of clinical improvement from *Crotalus adamanteus* envenomation treated at 49 hours following envenomation with Crotalidae Polyvalent Immune Fab Antivenom. **Case report:** A 19-year-old female presented to an emergency department in the south eastern US immediately after an Eastern Diamondback (*Crotalus adamanteus*) bite to her left ankle. Initial symptoms included vomiting, myokymia, and pain at the bite site. Vital signs were reported as normal and initial labs demonstrated a partial thromboplastin time (PTT) 33 seconds, international normalized ratio (INR) 1.04, platelets 250,000/ $\mu$ L, and fibrinogen 347 mg/dL. She did not receive antivenom and was discharged home following a 6-hour observation. She subsequently presented to her primary care physician 43 hours later with worsening edema, ecchymoses on her left lower extremity, and pain. Physical examination further revealed ecchymosis on her upper extremity where the blood pressure cuff was placed and persistent bleeding at the site of an intravenous catheter. Repeat laboratory tests included PTT greater than 200 seconds, INR greater than 18, platelets 260,000/ $\mu$ L, and fibrinogen less than 61 mg/dL. All laboratory values were repeated to ensure accuracy. She was treated with six vials of Crotalidae Polyvalent Immune

Fab antivenom 49 hours after envenomation. After four hours the PTT was 38 seconds, INR 5, platelets 239,000/ $\mu$ L, and fibrinogen less than 61 mg/dL. She received another two vials every six hours for three total treatments with resolution of swelling to her ankle. Prior to discharge she had a prothrombin time of 15.4 seconds, PTT 27.7 seconds, INR 1.24, platelets 201,000/ $\mu$ L and fibrinogen 225 mg/dL. She followed up with her physician one week later without any further symptoms. **Conclusion:** *Crotalus adamanteus* is endemic to the south eastern US and likely the cause of envenomation in this case due to the severe fibrinolysis and absence of thrombocytopenia. The utility of delayed Crotalidae Polyvalent Immune Fab antivenom following envenomation has not been well described. In our case, there was rapid improvement of both the edema and coagulopathy following delayed administration. The fact that *Crotalus adamanteus* is one of four species involved in the manufacturing of the fab fragments may have also contributed to the rapid resolution of the patient's symptoms. This case demonstrates potential efficacy previously not shown and antivenom should be considered in patients with delayed presentations following crotalinae envenomation.

### 326. Dangerous pets: Cape cobra (*Naja nivea*) envenomation in Barcelona

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**Objective:** To present a case of an envenomation from an exotic snake with neurotoxic venom.[1] In Spain the legislation on dangerous animals requires the animal's owner to hold the relevant antivenom (to ensure availability in an emergency). **Case report:** A 26-year-old man was bitten in his right hand by a Cape cobra while he was cleaning the reptile's cage in a private reptile collection near Barcelona. Soon after he started feeling anxious, had itching of the eyes, nasal discharge and sneezing. He called for medical attention and for the antidote he knew was at "Zoo de Madrid". First aid was provided by a pre-hospital medical team, whom administered 200 mg hydrocortisone intravenously (IV), 5 mg dexchlorpheniramine IV and morphine. He was then transferred to our hospital. On arrival, 45 minutes after the accident, he was pale with mild tachycardia, but both blood pressure and oxygen saturation on ambient air were normal. He had two needle-shaped fang marks on the dorsum of his right hand with little local oedema, and normal neurological examination. Symptomatic treatment was administered, while sourcing the antivenom. Four hours after the accident, he developed progressive dyspnoea and oxygen desaturation. The antivenom (S.A.I.M.R Polyvalent Antivenom) was obtained from a private exotic collection in Madrid and transported by plane to Barcelona. It was administered to the patient with a rapid improvement of his condition. He was discharged from the hospital 36 hours later, with oral antibiotic and anti-inflammatory treatment. He was seen in the outpatient clinic one and two weeks after the event, but had no complications. **Conclusion:** This is the first case report in the medical literature from Spain about envenomation from this non-native snake. It highlights the increase of non-regulated exotic snake owners in Europe and the importance of having national protocols to cope with these accidents and ensure availability of antivenom.[2,3]

### References

- [1] Blaylock RS, Lichtman AR, Potgieter PD. Clinical manifestations of Cape cobra (*Naja nivea*) bites. A report of two cases. S Afr Med J. 1985;68:342–344.
- [2] Warrick BJ, Boyer LV, Seifert SA. Non-native (exotic) snake envenomations in the US, 2005–2011. Toxins (Basel). 2014;6:2899–911.
- [3] Schaper A, Desel H, Ebbecke M, et al. Bites and stings by exotic pets in Europe: an 11 year analysis of 404 cases from Northeastern Germany and Southeastern France. Clin Toxicol (Phila). 2009;47:39–43.

### 327. Treatment of pain using only hot water baths after weever and scorpion fish envenomations on the French coast

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**Objective:** Fish envenomation, particularly weever fish (*Trachinus draco* and *Echiichthys vipera*) or scorpion fish (genus *Scorpaena*) are frequent along the coast of France, and although benign are responsible for intensive pain, due to injection of the thermolabile venom. Treatment currently recommended is thermal shock which consists of a variation in local temperature with heat then ice.[1] However, finding ice on the French coast during the summer is challenging. Moreover, treatment with only hot water has never been evaluated. The objective of this study was to evaluate the efficiency of a hot water bath (of the affected limb) on pain in patients after envenomation. **Methods:** A prospective study was conducted between 1 July and 31 August 2015 in which 10 volunteer lifeguard stations of the National Sea Rescue Society, located along the coast took part. All patients over 6 years old with weever fish envenomation and seen at one of the lifeguard stations with pain were included. On arrival, these patients received an evaluation of pain by a visual analogue scale (VAS), then a water bath as hot as possible without exceeding 42 °C (checked by thermometer) for 15 minutes, followed by a second evaluation of pain after the bath, then a third, 15 minutes later. Children younger than 6 years old, those with multiple stings and patients treated with analgesics in the previous 24 hours were excluded. **Results:** In total 178 patients were included. Stings occurred on the Mediterranean, Atlantic and Manche beaches with an average 10.46 minutes between sting and treatment. The sex ratio was 0.54 and the average age 26.78 years. Most patients (93.26%) were stung on a lower limb and 6.74% on an upper limb. The average VAS on the arrival was 5.93. The average water bath temperature was 40.55 °C and average duration was 14.48 minutes. The second VAS after 15 minutes was 2.07, and the last VAS evaluated 15 minutes after the end of bath was 1.36. The difference in pain is statistically significant ( $p < 0.001$ ). None of the patients required contact with a Poison Center or emergency medical call center. **Conclusion:** Treatment with only and exclusive a hot water bath can reduce pain after weever or scorpion fish stings.

## Reference

- [1] De Haro L, Prost N, Arditi J, et al. Efficacy of local temperature variation in the treatment of Mediterranean fish envenomations: experience of the Marseilles Poison Center during the summer of 1999. *J Eur Urgences*. 2001;14:171–173.

## 329. Sea snake envenoming in Australia causes myotoxicity, local effects and non-specific systemic symptoms (ASP-24)

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**Objective:** Sea snake envenoming is a rare and poorly characterised clinical syndrome in Australia. Isolated case reports from Australia describe neurotoxicity and myotoxicity, but most are unconfirmed cases.[1,2] The aim of this study was to describe the epidemiology, clinical presentation and treatment of sea snake envenoming in Australia. **Methods:** Patients are recruited to the Australian Snakebite Project (ASP), an ongoing multi-centre observational study of snakebite Australia-wide. ASP uses predefined data collection, laboratory investigations and venom assays to describe envenoming. Data collection sheets and laboratory protocols are faxed to clinicians who return them by fax. In this analysis we included patients with sea snake bites. **Results:** From September 2005 to October 2015 there were seven patients with confirmed sea snake bites from a total of 1685 patients recruited to ASP. The median patient age was 23 years (4–62 years); six patients were male. All bites occurred in the wild, six in north Queensland and one off the West Australian coast. All patients were in the water or fishing when bitten, including four fishing or working with fishing nets. Two bites occurred at night. Local effects occurred in six patients with pain ( $n=4$ ), swelling ( $n=4$ ) and bruising ( $n=1$ ). Five patients had systemic envenoming. Four had non-specific systemic effects with headache ( $n=4$ ), nausea ( $n=3$ ), abdominal pain ( $n=2$ ) and generalised diaphoresis ( $n=1$ ). Four patients had myotoxicity: one had generalised myalgia, two had local myalgia only and one had no myalgia. Median peak creatine kinase was 14,570 IU/L (range 804–48,100). No patients with myotoxicity developed renal impairment. Coagulopathy and neurotoxicity did not occur. Three patients with envenoming had elevated white cell counts on presentation ( $10.4$ ,  $14.2$  and  $15.7 \times 10^9$ ). One vial of sea snake antivenom (CSL Ltd) was given to four patients; one patient receiving a second vial. One patient had a systemic hypersensitivity reaction to antivenom with urticaria, generalised erythema and nausea treated with promethazine, ondansetron, intramuscular adrenaline and an adrenaline infusion. Median length of hospital stay was 16.5 hours (range 8.5 to 84 hours). **Conclusion:** Sea snake envenoming is rare in Australia and is characterised by local effects, non-specific systemic effects and mild to moderate myotoxicity.

## References

- [1] Sutherland SK, Tibballs J. Family Hydrophiidae, Sea Snakes. In: Sutherland SK, Tibballs J. *Australian Animal Toxins*. 2nd ed. Oxford, England: Oxford University Press; 2001:247–285.
- [2] Fulde GW, Smith F. Sea snake envenomation at Bondi. *Med J Aust*. 1983;141:44–45.

## 330. The French snake antivenom bank

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**Objective:** Exotic pets have become fashionable in France. Venomous snakes are undoubtedly the most dangerous exotic pets. Since ownership of venomous snakes is never risk free, all owners, both professional and non-professional (licensed and unlicensed), are likely to be bitten at some point with potentially life-threatening consequences. At present, the only effective specific treatment is antivenom therapy. When indicated, the correct dose must be administered intravenously as soon as possible.[1] In light of the growing risk of envenomation and the need to comply with regulations on the supply, storage and distribution of snake antivenom, a Snake Antivenom Bank was set up. **Methods:** The main aim of the Bank was to develop a medical treatment programme for patients bitten by exotic snakes in mainland France, along with a hospital pharmacy to manage the active antivenoms used for these species. **Results:** The Bank comprises four sites holding snake antivenoms (Viperfav<sup>®</sup>, Bothrofav<sup>®</sup>, Favafrigue<sup>®</sup>, Antivipmyn-tri<sup>®</sup>, Favirept<sup>®</sup>) that meet the quality and viral safety criteria established by the evaluation division of the French National Agency for the Safety of Medicine and Health Products. The antivenoms can treat over 40 different types of envenomation (covering European, African and American snake species), out of a total of 93 exotic species known to be present in France. Since 2007, the Bank has been consulted to treat 11 cases of envenomation in professionals and unlicensed amateur breeders, seven of whom (*Daboia palaestinae*, *Crotalus polystictus*, *Naja annulifera*, *Crotalus durissus*, *Bothriopsis taeniata*, *Bitis arietans*, *Dendroaspis viridis*) had moderate to severe envenomation that was successfully treated with antivenom, with no sequelae. In all cases, the antivenoms were delivered in under six hours: the recommended time limit between being bitten and the administration of antiserum. Long-term follow up of these patients confirmed that the antivenoms were well tolerated. **Conclusion:** The Bank currently operates as a network, which has reduced resupply costs resulting from the antivenoms expiring, as well as cutting delivery times across France. The Bank and its network of experts, including members of the association, also keep a record of venomous species present in France, work to improve treatment for envenomation and help poison control centres collect data on envenomation for the purposes of toxicovigilance and public health surveillance.

## Reference

- [1] Boels D, Hamel JF, Bretaudeau Deguigne M, et al. European viper envenomings: Assessment of Viperfav<sup>TM</sup> and other symptomatic treatments. *Clin Toxicol (Phila)*. 2012;50:189–196.

### 331. Hot water immersion treatment for lion's mane jellyfish stings in Scandinavia

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**Objective:** There are a number of different treatment options for jellyfish stings in Nordic sea waters.[1–2] Hot water immersion therapy (HWI) has not been investigated previously after lion's mane jellyfish stings. The objective of this study was to evaluate the effect of HWI compared to standard treatment with topical lidocaine after stings with lion's mane jellyfish (*Cyanea capillata*). It was also the objective to visualize the effects of different suggested treatments on nematocysts *in vitro*. **Methods:** Eighteen healthy volunteers were exposed to fresh lion's mane jellyfish at each ankle. Twenty minutes after exposure one leg was treated with HWI (45 °C for 30 minutes) and the other leg with topical administration of lidocaine (5%). Pain and itching were measured on a Visual Analogue Scale (VAS) directly after exposure and repeated after 30, 60 minutes and 24 hours. The effect of different treatment options was also examined in an *in vitro* setting to evaluate the firing of nematocysts under the microscope. **Results:** Pain and itching after skin contact with lion's mane jellyfish was present but not intense in all subjects. Both lidocaine and HWI reduced pain and itching effectively. At time 0, just before HWI started, the mean VAS score was 1.8, and the mean itch score 3.4. HWI was significantly more effective than lidocaine in reducing both pain and itching 30 minutes after exposure. At 30 minutes, the mean VAS score was 0.5 for the leg treated with HWI, and 1.3 for the lidocaine-treated leg ( $p < 0.05$  Wilcoxon signed-rank test). After 24 hours very few symptoms remained but more subjects felt some itching after lidocaine than after HWI. In the *in vitro* setting vinegar caused a visible firing of nematocysts whereas lidocaine did not. **Conclusion:** Both lidocaine and HWI seem to be effective in reducing symptoms after dermal contact with lion's mane jellyfish. HWI was more effective in reducing symptoms and seems to be an easy accessible treatment for these stings. Vinegar causes firing of the nematocysts *in vitro* and does not seem to be a recommendable treatment option.

#### References

- [1] Birsa LM, Verity PG, Lee RF. Evaluation of the effects of various chemicals on discharge of and pain caused by jellyfish nematocysts. *Comp Biochem Physiol C*. 2010;151:426–430.
- [2] Isbister GK. Managing injuries by venomous sea creatures in Australia. *Aust Prescr*. 2007;30:117–121.

### 332. Antivenom availability and clinical response to treatment in viper envenomation in Italy: 3 years' preliminary experience

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**Objective:** EU marketed viper antivenoms differ in pharmaceutical characteristics (e.g. Fab/F(ab')<sub>2</sub>, equine/ovine, *Vipera* species. neutralizing activity), dosage and administration route. A different availability in Italian hospitals offers the opportunity to evaluate the relative frequency of use and clinical response to treatment with four different antivenoms. **Methods:** All viper bitten patients treated with antivenom referred to Pavia Poison Control Centre from 2013 to October 2015 were retrospectively assessed for sex, age, site of bite, time elapsed between bite and emergency department (ED) admission/antivenom administration, antivenom type, number of vials, Glasgow Coma Scale (GCS) and clinical response (improvement/worsening during 6 hours), need of additional doses, adverse effects. Clinical manifestations were evaluated according to the Grading Severity Score (GSS). **Results:** In total 50 patients (age 44.3 ± 27.2 years; male 70%) were included; 13 were paediatric (1–13 years). *Vipera aspis* was the most common snake involved. Upper and lower limbs were involved in 88% and 12% of cases, respectively. Average time between bite and ED admission was 4 hours (0.25–23 hours), and 9 hours (0.67–26 hours) between bite and antivenom administration, that occurred in patients with GSS 2 or 3 (76% and 24%, respectively). The four antivenoms were administered intravenously: Viper Venom Antiserum-European® (VVAE) (30/50; 60%, 7 = 1 vial, 23 = 2 vials), Viper Venom Antitoxin® (VVA) (16/50; 32%, 11 = 1 vial, 5 = 2 vials), ViperaTab® (3/50; 6%, 2 vials) and Viekin® (1/50; 2%, 1 vial). Clinical improvement was observed after 1 and 2 vials of VVAE administration in 86% and 96% of cases, respectively, and after 1 and 2 vials of VVA in 55% and 80% of cases. ViperaTab® treated patients ( $n = 3$ ) improved in 66.6%. One patient (9-years-old) treated with Viekin® promptly recovered. Adjunctive doses of antivenom were needed in 6 patients (12%) aged 2 to 6 years (except one aged 49 years) that received only 1 vial of VVAE (1/6; 16%) or VVA (5/6; 83%). Acute adverse reactions occurred after VVAE (2 cases; angioedema, pruritus) and VVA administration (1 case; mild hypotension). Serum sickness (3 weeks later) occurred in 1 case (VVA). Statistical evaluation requires a greater number of cases. **Conclusion:** Different availability of four antivenoms was observed in Italian hospitals, with a prevalence of those that declare neutralizing activity against *Vipera aspis*. Intravenous administration is usually safe, even if adverse reactions are observed. An initial dose of 2 vials of all formulations is suitable to reduce the probability of worsening symptoms and the need of adjunctive doses, especially in paediatric patients.

### 333. Cardiac magnetic resonance findings in myocarditis due to scorpion envenomation

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**Objective:** Scorpion envenomation is considered a major public health problem in tropical, subtropical and sub-Saharan areas.

Scorpion  $\alpha$ -toxins inhibits voltage-gated sodium channel inactivation resulting in prolonged depolarization and, finally, neuronal excitation with adrenergic and cholinergic excess. The main mechanisms of cardiac dysfunction and pulmonary edema related to scorpion envenomation are multifactorial. The vasoactive effect of catecholamine and biochemical mediators cause cardiac overload and contribute to acute cardiac failure or myocardial ischemia or myocarditis. We describe the evolution of a toxic myocarditis documented at four repeated cardiac magnetic resonance (CMR) scans during follow up. **Case report:** A 25-year-old woman was stung on the foot by a *Leiurus quinquestriatus* scorpion on a Red Sea beach (Egypt). At admission 2 hours later, she presented with normal blood pressure, local acute pain, fever (38 °C), tachycardia (117 bpm) associated with dyspnea and diffuse pulmonary rales. Chest radiography evidenced severe pulmonary edema, and echocardiography assessment revealed significant deterioration of left ventricle (LV) systolic function, with global hypokinesia and left ventricle ejection fraction (LVEF) of 25%. Biochemistry showed an increase of troponin I (6.16  $\mu$ g/L), CPK-MB (97 U/L), amylase (220 U/L) and lactate dehydrogenase (LDH) (558 IU/L) associated with leukocytosis and thrombocytopenia. She was treated with prazosin, dobutamine, furosemide, hydrocortisone, levofloxacin, a proton pump inhibitor, acetaminophen, a non-steroidal anti-inflammatory, clindamycin and enoxaparin. Purified Polyvalent Antiscorpion Serum was administered. Her clinical condition progressively improved with normalization of myocardial necrosis indices and LVEF (67%) within 9 days. The patient was transferred to our hospital 11 days after the bite. Echocardiography was normal except for systolic pulmonary pressure at the upper limit level. Repeated CMR evaluations (11 days; 3, 9 and 16 months) were performed. ECG-gated cine images, assessed by a steady-state-free precession sequences, showed normal LV volumes and LVEF at baseline, and mild worsening of LVEF during the follow up (53 to 60%). Significant early uptake of gadolinium at T1-weighted turbo spin-echo (TSE) sequence, suggesting myocardial inflammation, was revealed at baseline, and gradually reduced during follow up, particularly between the 6th and 9th months. Irreversible myocardial damage was assessed by late enhancement technique, which revealed mild intra-myocardial and sub-epicardial late enhancement that persisted in follow up. **Conclusion:** Our experience supports the hypothesis that excess catecholamine is crucial in the pathophysiology of cardiac dysfunction observed in stress-induced cardiomyopathy and scorpion envenomation. CMR evaluation is useful to monitor sub-clinical myocardial alterations considering the possible evolution to dilated cardiomyopathy.

### 335. Snakebite and use of three antivenoms in Morocco: FAV-Afrique<sup>®</sup>, Favirept<sup>®</sup> and Inoserp<sup>®</sup> MENA

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**Objective:** In Morocco, incidence of snakebite envenomation is estimated at 0.2/100,000 inhabitants and the case fatality rate reaches 7.2%. The most medically important snakes are *Macrovipera mauritanica*, *Bitis arietans*, *Cerastes cerastes*, and *Naja haje legionis*. Antivenom therapy is the only effective treatment in

severe cases. Local production of antivenom in Morocco stopped in 2002 and the Moroccan Poison Control Center (MPCC) strategy is to acquire antivenom targeting the most venomous snakes in Morocco. Three antivenoms are available: FAV-Afrique<sup>®</sup> since 2012 (active against *Echis*, *Naja*, *Bitis*), Favirept<sup>®</sup> and Inoserp<sup>®</sup> MENA since 2015 (both active against all four of the most medically important snakes). The aim of this study was to analyse cases of snake bite and usage of these three antivenoms. **Methods:** This is a retrospective study over a period of 4 years (January 2012 to September 2015), involving all the reported cases of snakebite to the MPCC. Cases were reported by three different forms and report: Intoxication Declaration Forms (IDF), Information Toxicological Forms (ITF) which are filled out during telephone calls from both the public and health professionals and "copy of the specific hospital report", established since August 2012. We analyzed the cases that received antivenom FAV-Afrique<sup>®</sup> and Favirept<sup>®</sup> both produced by Sanofi Pasteur and Inoserp<sup>®</sup> MENA produced by Inosan. In cases where the snake was formally identified, the MPCC recommended the most specific antivenin. **Results:** During the study period, 810 cases of snakebites (annual mean 202 cases) were notified to the MPCC. The overall case fatality rate was 4.6% (37 deaths); 30 patients who died did not receive antivenom. FAV-Afrique<sup>®</sup> antivenom was administered to 86 patients. The outcome was good in 81 patients while 5 died. Favirept<sup>®</sup> was administered to 14 patients. The outcome was good in all patients. Inoserp<sup>®</sup> MENA was administered to 23 patients. The outcome was good in 21 patients while 2 died. There were two cases of anaphylactic shock reported with FAV-Afrique<sup>®</sup> and two with Inoserp<sup>®</sup> MENA. The analysis of variance of the administration of three antivenoms according to the case evolution showed a highly significant difference ( $p < 0.001$ ) between Favirept<sup>®</sup> and the two other antivenoms. **Conclusion:** Favirept<sup>®</sup> was effective and safe but the production of this and FAV-Afrique<sup>®</sup> has ceased. The alternative would be to continue importing Inoserp<sup>®</sup> MENA which targets the most venomous snakes of Morocco. Close monitoring and follow up of all cases who receive Inoserp<sup>®</sup> MENA is essential.

### 336. Oven cleaner exposure in pets

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**Objective:** To determine the clinical signs and outcomes associated with exposure of household pets to oven cleaners. These products typically contain strong alkalis such as sodium or potassium hydroxide which can cause significant tissue injury. **Methods:** Retrospective analysis of cases of oven cleaner exposure in animals reported to the VPIS. Only cases with returned veterinary surgeon follow up (via postal questionnaire) were included. **Results:** There were 87 cases involving 69 dogs, 17 cats and 1 rabbit. Of these 21 animals remained asymptomatic (24%). Of the symptomatic cases ( $n = 66$ ), 22 has gastrointestinal signs with oral irritation, ulceration and/or burns, 17 has mild gastrointestinal signs but no burns, 16 showed skin irritation, ulceration and/or burns, 7 animals had both skin and oral burns and four animals had ocular irritation or ulceration. The most common signs were skin burns ( $n = 18$ ), tongue ulceration ( $n = 10$ ), hypersalivation ( $n = 10$ ) and vomiting ( $n = 10$ ). The circumstance of exposure was described in a free text field and was most commonly licking the cleaner off the oven ( $n = 8$ ) or a spill or drips from the oven ( $n = 7$ ). Other animals were exposed after a spill on the skin ( $n = 3$ ), chewing the container ( $n = 3$ , in one case it was chewed after delivery through the post) and sitting in a spillage ( $n = 2$ ). One dog was exposed when treated oven shelves

were left to soak on top of its cage and the cleaner dripped through causing oral and skin burns. One dog died (with shock and respiratory distress) but all other animals recovered. Healing was slow in some cases with a mean recovery time of 10.2 days ( $n=18$ ) and a range of 3 hours to 6 weeks. The dog that took 6 weeks to heal had severe burns (down to the pelvic bone) that developed after it sat in the cleaner. Sequelae in two dogs were thickening of the skin and scarring. **Conclusion:** Pets can be exposed to oven cleaners during use, particularly where the product has been left to soak off burnt food debris. Sitting in a spill of oven cleaner can cause severe injury because alkali injuries can initially be painless and result in deep tissue penetration. Owners need to be aware that product safety warnings also apply to their pets; manufacturers could improve labelling in this regard. It is essential to clean up spills promptly and limit access to treated ovens.

### 337. Sodium hypochlorite bleach exposure in dogs

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**Objective:** Sodium hypochlorite bleach is a commonly used household cleaning agent. These household bleaches are typically approximately 5% sodium hypochlorite. Exposure usually causes mucosal irritation and more rarely burns. Hypernatraemia and hyperchloraemia may also occur.[1] The clinical signs, treatment and outcomes in dogs exposed to sodium hypochlorite bleach reported to the VPIS were reviewed. **Methods:** A retrospective analysis of canine cases of exposure to sodium hypochlorite bleach reported to the VPIS. All cases with exposure to bleach as a single agent and known outcome with returned veterinary surgeon follow up (via postal questionnaire) were included. **Results:** There were 130 cases of bleach exposure in dogs with follow up reported to the VPIS. Of these 62 (48%) remained asymptomatic. Ingestion occurred in 95.4% ( $n=124$ ) of cases. The majority of symptomatic dogs developed only gastrointestinal signs ( $n=53/68$ ); 7 had respiratory signs (cough, tachypnoea, panting, aspiration pneumonia), 7 developed dermal effects (erythema, skin irritation) and 2 had ocular signs. The most common signs overall were vomiting ( $n=25$ ) and hypersalivation ( $n=15$ ). Oral or tongue ulceration or burns occurred in 7 dogs. Both dogs with ocular exposure developed conjunctivitis. Electrolyte disturbances were not reported in any case. The estimated volume ingested ranged from 5 ml to 1 litre, but there was no association between the volume estimated to have been ingested and the clinical signs reported. Treatment in symptomatic dogs ( $n=68$ ) was supportive; 24 dogs were given a gastroprotectant, 21 received sucralfate and 35 were rehydrated (18 receiving oral fluids and 17 given intravenous fluids). Only one dog was given an emetic; it developed no clinical signs or adverse effects. There was only one fatal case: a dog was euthanized after developing vomiting, diarrhoea and oral burns. Based on this, the fatality rate was 0.8%. All the other dogs recovered fully. **Conclusion:** Although severe sodium hypochlorite poisoning has been reported in dogs,[1] this is rare and many dogs that ingest bleach remain well. Those that do develop signs typically have gastrointestinal effects; respiratory and dermal signs are less common. Conservative treatment is sufficient in the majority of cases; emesis has no role in the management of sodium hypochlorite bleach ingestion in dogs.

### Reference

- [1] Chapman S, Pittman J, Johnson M, et al. Sodium hypochlorite bleach ingestion in two dogs. *Vet Med.* 2008;103:13–18.

### 338. A retrospective study of household battery exposure in 271 dogs

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**Objective:** To determine the clinical signs and outcome in dogs exposed to household batteries. **Methods:** A retrospective study of 271 cases of battery exposure in dogs reported to the VPIS between February 1987 and August 2015. **Results:** Following household battery exposure, 53.5% of dogs ( $n=145$ ) remained asymptomatic. Of the symptomatic dogs, vomiting was the predominant sign seen in 26.6% ( $n=72$ ) of cases. Oral ulceration or inflammation was evident in 16.6% ( $n=45$ ). Hypersalivation or frothing at the mouth (11.4%), lethargy/depression (8.5%) and inappetence/anorexia (4.4%) were other frequently reported clinical signs. In one case hepatic damage was reported, although the dog made a full recovery with supportive care. Of the cases involving ingestion, 10% ( $n=23/230$ ) involved button batteries, 32.2% ( $n=74$ ) AA batteries, 19.1% ( $n=44$ ) AAA batteries and 38.7% ( $n=89$ ) were of unknown batteries. Where known, the average time for batteries to be passed in faeces was 51 hours (minimum within 24 hours, maximum one week post-ingestion), with the majority (81.3%,  $n=13/16$ ) passed within 48 hours. Surgical or endoscopic removal of ingested batteries was undertaken in 14 cases (6.08%); a gastrotomy was undertaken to remove a button battery, there were four surgical cases involving AA batteries, four involving AAA batteries and five cases whereby surgery was undertaken to remove batteries of unknown type. In all but one of these surgical cases the dogs recovered. Overall there were two fatalities. An adult dog developed ataxia, melaena, vomiting and convulsions after ingestion of an unknown battery and died within 24 hours. The second fatality involved a bulldog that underwent a laparotomy to remove an unknown battery ingested six days previously. The battery had not corroded, but there was intestinal ulceration, haematuria and jaundice. Of 41 cases involving only buccal exposure 43.9% ( $n=18$ ) involved AA batteries, 4.9% ( $n=2$ ) AAA batteries and 51.2% ( $n=21$ ) unknown batteries; 21.95% ( $n=9$ ) of dogs remained asymptomatic, with 36.6% ( $n=15$ ) developing oral ulceration/inflammation, 24.4% ( $n=10$ ) hypersalivation, 19.5% ( $n=8$ ) vomiting and 12.2% ( $n=5$ ) with lethargy/depression. The maximum time to recovery from buccal exposure was four days. **Conclusion:** Battery exposure in small animals may cause oral ulceration, respiratory effects and oesophageal or gastrointestinal ulceration and perforation, although ingested batteries commonly pass uneventfully through the gastrointestinal tract.[1] In this series, the effects in symptomatic animals were predominately oral ulceration/inflammation and vomiting; there were no cases of gastrointestinal obstruction and the overall fatality rate was low (0.73%).

### Reference

- [1] Gwaltney-Brant S. Household and industrial products. In: Plumlee KH, ed. *Clinical Veterinary Toxicology*. St Louis, USA: Mosby; 2004:140–142.



### 339. Severe acute 1,2-dichloropropane poisoning involving sheep

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**Objective:** Poisonings can be of various severity and they involve not only humans but also different species of animals. Generally, animal intoxications are accidental; they are not endowed with reason so the risk of poisoning is more common. Usually the exposure is oral, although contact with the toxic agent can occur in different ways. Sometimes the poisoning is due to human negligence. We describe an incident of severe poisoning due to acute skin exposure involving 12 sheep. **Case report:** A toxicological request concerning sheep arrived at the Poison Control Centre from a veterinarian. A farmer was about to shear his sheep but, seeing the dirty fleeces, decided to clean them using a household stain remover in order to facilitate shearing. This product is usually used as a clothes stain remover. The day after the exposure, all sheep were found lying down with serious difficulties in movement and breathing. The skin, eyes, and the mucous membranes appeared severely oedematous. Waiting for veterinary intervention, the fleeces had been strewed with white mineral oil and then washed in water with Marseille soap. In total 12 sheep had been exposed and the dose of stain remover used was 1500 ml (three 500 ml containers). The product was composed of a mixture of 1,2-dichloropropane, hexane, and cyclohexane. The latency period between the time of exposure and the time of the request was approximately 12–18 hours. During this time, the toxic agent was absorbed through the skin and by inhalation, causing signs consistent with severe solvent exposure. The sheep were laterally recumbent, unresponsive to pain and had seizures. Unfortunately, all the animals died within a few days of exposure. There was no post-mortem examination. **Conclusion:** 1,2-dichloropropane is the most toxic of the three components of the stain remover. It is a colourless flammable liquid with a chloroform-like odour and is contained in many commercial products, such as solvents for oils, waxes, resins and glues, degreasing and dry-cleaning fluids, pesticides, lead scavengers for gasoline, and paint fixatives.[1] Exposure to this chemical can cause severe signs with effects on the central nervous system, lungs, heart, liver, kidney and bone marrow.

#### Reference

- [1] Fiaccadori E, Maggiore U, Rotelli C, et al. Acute renal and hepatic failure due to accidental percutaneous absorption of 1,2-dichloropropane contained in a commercial paint fixative. *Nephrol Dial Transplant.* 2003;18:219–220.

### 340. Chocolate poisonings in dogs: a consecutive case series

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**Table 1.** Severity of clinical course in dogs according to the theobromine dose ( $n = 113$ ).

Severity	Milk chocolate		Dark chocolate	
	≤60 mg/kg theobromine	>60 mg/kg theobromine	≤60 mg/kg theobromine	>60 mg/kg theobromine
Asymptomatic	41	0	20	12
Minor	14	2	4	8
Moderate	0	2	1	7
Severe	0	0	0	2

**Objective:** Chocolate is a common cause of canine poisoning. The main toxic compound is theobromine and severe signs in dogs have been reported with 40–60 mg/kg.[1] The aim of this study was to determine a critical value of theobromine, which distinguishes between a minor and a severe course. **Methods:** Retrospective analysis of well documented canine exposures to milk or dark chocolate reported to two poisons centres (January 2002 to July 2015). To calculate the quantity of theobromine we multiplied the amount of milk chocolate by a factor of 0.0015 and the amount of dark chocolate by a factor of 0.0115. These factors were derived from the mean of typically reported theobromine contents of milk (1–2) and dark chocolate (7–16). The severity was evaluated according to the Poisoning Severity Score. **Results:** Of 122 dogs the ingested amount was known in 113, 59 consumed milk chocolate and 54 dark chocolate (Table 1). Gastrointestinal decontamination (emesis and/or activated charcoal) was performed in 30/59 dogs who ingested milk chocolate and in 36/54 dogs who ingested dark chocolate. Asymptomatic dogs ingested 1.3–33.3 g/kg (mean 11.3, median 10.4) milk chocolate ( $n = 41$ ) or 0.7–33.3 g/kg (mean 6.5, median 4.1) dark chocolate ( $n = 32$ ). Minor signs were observed after ingestion of 4.2–80 g/kg (mean 28.3, median 23.8) milk chocolate ( $n = 16$ ) or 3.1–13.9 g/kg (mean 7.6, median 7.4) dark chocolate ( $n = 12$ ). Moderate signs were observed after 42.9 and 47.6 g/kg milk chocolate ( $n = 2$ ) or 5.0–30.0 g/kg (mean 18.0, median 15.5) dark chocolate ( $n = 8$ ). Severe signs occurred in two dogs after ingestion of 11.1 and 50.0 g/kg dark chocolate. There were no fatalities. **Conclusion:** Clinical course after ingestion of chocolate by dogs is usually asymptomatic or minor. Ingestion of up to 60 mg/kg theobromine did not induce life-threatening signs. This corresponds to about 40 g/kg milk chocolate or 5.2 g/kg dark chocolate.

#### Reference

- [1] Gwaltney-Brant S. Chocolate intoxication. *Vet Med.* 2001;96:108–111.

### 341. Can fastidiousness kill the cat? Detergent exposures in cats: a common cause of respiratory effects

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**Objective:** The toxicity of detergents varies, but they all reduce surface tension and are associated with a risk of respiratory signs from foam aspiration. In humans, detergent exposure is common, but respiratory effects uncommonly reported,[1,2] unless large amounts are ingested.[3] We examine the prevalence of respiratory signs in cats following exposures to detergents.

**Table 1.** Incidence of respiratory effects in cats after detergent exposure in cases reported to the VPIS.

Clinical effect	Number of cats	Percentage of 341 cases
Tachypnoea	20	5.87
Dyspnoea	18	5.28
Lung sounds abnormal	18	5.28
Respiratory distress	11	3.23
Cough	9	2.64
Respiration laboured	9	2.64
Nasal discharge	6	1.76
Wheezing	5	1.47
Pulmonary congestion	3	0.88
Pulmonary oedema	3	0.88
Cyanosis	2	0.59
Hyperventilation	2	0.59
Aspiration pneumonia	1	0.29
Stridor	1	0.29

**Methods:** Retrospective analysis of feline detergent exposures reported to the Veterinary Poisons Information Service (VPIS), including all cases of ionic, cationic and non-ionic detergents with follow up from 1985 to November 2015. **Results:** In total there were 32,662 feline cases reported in this period. Of these 341 (1.04%) involved a detergent or detergent-containing product (all but two were cleaning or disinfectant products). Respiratory effects were commonly reported, occurring in 26% ( $n=88$ ) of cats (Table 1). In addition seven cats died or were euthanized (1.5%); all has respiratory signs but two had confounding factors (hypertrophic cardiomyopathy and undiagnosed neurological disease). **Conclusion:** Respiratory damage from detergent ingestion is frequently claimed but rarely reported. In this series severe effects were uncommon, but there was a high incidence of respiratory signs in cats, perhaps due to their fastidious grooming habits [4] which puts them at risk.

## References

- [1] McKenzie LB, Ahir N, Stolz U, et al. Household cleaning product-related injuries treated in US emergency departments in 1990–2006. *Pediatrics*. 2010;126:509–516.
- [2] Williams H, Jones S, Wood K, et al. Reported toxicity in 1486 liquid detergent capsule exposures to the UK National Poisons Information Service 2009–2012, including their ophthalmic and CNS effects. *Clin Toxicol (Phila)*. 2014;52:136–140.
- [3] Schaper A, Renneberg B, Desel H, et al. Intoxication-related fatalities in northern Germany. *Eur J Intern Med*. 2006;17:474–478.
- [4] Read JL. Can fastidiousness kill the cat? The potential for target-specific poisoning of feral cats through oral grooming. *Ecol Manag Restor*. 2010;11:230–233.

## 342. Severe zinc intoxication in a dog: a case report

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**Objective:** Animals can be involved in exposures to chemical compounds of various natures. Herein is described a particularly severe case regarding a dog that was thought to have ingested a

tablet used to disinfect swimming pools but it was later discovered that the symptomatology was consistent with zinc poisoning. **Case report:** The poison centre was consulted about a Jack Russell Terrier dog weighing approximately 7 kg who experienced sudden onset severe gastroenteric signs, with lack of appetite, diarrhea characterized by greenish feces and physical weakness, pallor in the conjunctival sac, rapidly worsening anemia, hemorrhagic urine with brown sediment and with completely hemolyzed serum. The caller explained that a few hours earlier the dog might have ingested a tablet used to disinfect the swimming pool. The tablet contained sinclosene (trichloroisocyanuric acid), copper and aluminium sulphate. The dog was also vaccinated 72 hours prior to the call. Many factors about this case made the sinclosene tablet a doubtful culprit at best, including the presence of such a severe anemia without gingival bleeding, the absence of signs of irritation of the mucous membranes, no angioedema type reaction to the vaccination, and, the absence of the typical renal failure associated with haemolysis and greenish feces. After having established a symptomatic therapy with cortisone, a blood sample was obtained from the animal, along with an abdominal X-ray. The X-ray revealed the presence of two foreign bodies in the stomach which were thought to be a pair of buttons ingested by the dog while chewing a pair of rubber slippers at an unspecified time in the past. The foreign bodies were removed surgically and the analysis revealed a high zinc plasma concentration (22.5 mg/L). The copper concentration was not measured. The signs persisted for approximately three weeks and the administration of cortisone was not discontinued until two months later. No chelation therapy was necessary. **Conclusion:** The animal presented with signs typical of zinc intoxication, so it is possible to assume with some certainty that the metal in the foreign body was zinc. The ingestion of zinc can cause not only irritation but also vomiting, epigastric pain, haematemesis, diarrhea, central nervous system depression and renal damage. Severe intravascular haemolysis is the most consistent clinical finding in acute zinc poisoning in dogs.[1]

## Reference

- [1] Meurs KM, Breitschwerdt EB, Baty CJ, Young MA. Postsurgical mortality secondary to zinc toxicity in dogs. *Vet Hum Toxicol*. 1999;33:579–583.

## 343. Severe animal poisonings by fertilizers composed of *Ricinus communis*: a case series

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**Objective:** Many kinds of fertilizers are available on the market; they are important for plant growth and to improve chemicophysical characteristics of the soil. Fertilizers contain the correct nutrient supply for plant growth and are usually composed of animal and vegetable residues and hold both micro and macro elements. Accidental ingestion is not usually the cause of serious poisoning. Some professional fertilizers used by farmers are composed of residual material of the castor bean plant *Ricinus communis* (RC). During the pressing of seeds the toxic molecules do not pass in solution and the castor bean cake holds a large

amount of nitrogen, carbon, phosphorus pentoxide, potassium and magnesium oxide as well as ricin. Moreover the release of these substances in the soil has an antagonistic effect against insects and parasites. Ricin is cytotoxic; in humans the fatal oral dose is 0.5 g/kg while in animals it is 1–2 g/kg.[1] We present the experience of the Poison Control Centre, Milan concerning animal poisoning due to RC-based fertilizers from 2003 to 2014. **Case series:** Over the study period, there were 7 cases of definite exposure to RC fertilizers and another 18 cases here it was not certain that RC was present in the fertilizer, however, the signs were similar to those seen with ricin poisoning, which suggests RC was present. All exposures were accidental oral ingestions, and concerned dogs which ingested the material from the product container. Clinical signs appeared after more than 24 hours ( $n = 12$ ; 48.0%). The most common signs were gastrointestinal ( $n = 12$ ; 48.0%) with vomiting and diarrhea (sometimes hemorrhagic diarrhea) in addition to depression and convulsions ( $n = 11$ ; 44.0%). Three dogs died about one day after ingestion; death was rapid after onset of signs. **Conclusion:** Most fertilizers have no toxic effects (if used properly) except those that contain RC. In this case the risk of severe poisoning is high for both animals and humans. Therefore, it is important to raise awareness of this potential hazard and to keep fertilizers in a safe place out of the reach of children and pets in order to reduce the risk of poisoning.

## Reference

- [1] Roels S, Coopman V, Vanhaelen P, et al. Lethal ricin intoxication in two adult dogs: toxicologic and histopathologic findings. *J Vet Diagn Invest.* 2010;22:466–468.

## 344. Salbutamol exposure in dogs

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**Objective:** Salbutamol is a selective beta2-adrenoceptor agonist, used as a bronchodilator. Exposure typically causes rapid onset tachycardia, tachypnoea, and more rarely hypokalaemia. Thermal injury consistent with exposure to released compressed gas from an inhaler has been reported.[1] The clinical signs, treatment and outcomes in dogs exposed to salbutamol reported to the Veterinary Poisons Information Service (VPIS), were reviewed. **Methods:** A retrospective analysis of all canine cases of salbutamol exposure reported to the VPIS between February 1985 and October 2015. All cases with exposure to salbutamol as a single agent and known outcome with returned veterinary surgeon follow up (via postal questionnaire) were included. **Results:** There were 411 cases of salbutamol exposure in dogs with follow up. Of these 20 (7%) remained asymptomatic, 4 of which received an emetic. Route of exposure was: not specified (42% of cases), chewing and puncturing an inhaler (48%) or ingestion of oral formulations (9%). Dose was known in 8 cases and ranged from 0.08 to 23.5 mg/kg; all of these dogs were symptomatic. The most common signs were tachycardia (78%), tachypnoea (20%), vomiting (19%), lethargy (16%), panting (16%), hypokalaemia (14%) and tremor (12%). Onset of signs was within 2 hours of exposure in 84% of cases (range 2 minutes to 12 hours). Duration of signs was 6 hours to 6 days, but 75% of dogs recovered within 24 hours. Hypokalaemia occurred in 59 dogs, value was known in 17 cases (range 2.4–3.6 mmol/L, normal range 3.9–5.1 mmol/L); 15 had associated weakness, twitching or collapse. While there were no reports of thermal injury, 17 dogs had signs of facial, oral or ocular inflammation (4% of cases). Of symptomatic cases ( $n = 382$ ), 109 (29%) received no treatment or observation only; 33 dogs

(9%) received gastrointestinal decontamination with an emetic or adsorbents. The most common treatments were beta-blockers (35%), IV fluids (16%), potassium (13%) and diazepam (11%). Of dogs with hypokalaemia 88% received treatment with potassium (24%), a beta-blocker (31%), or a combination of both (34%). One displayed cyanosis, hypersalivation, tachycardia, tachypnoea and died within 2 hours despite treatment with acepromazine, propranolol and oxygen; another died despite IV fluid therapy after presenting with tachycardia, shock and poor peripheral circulation. One case was ongoing at time of follow up and all other dogs recovered fully. **Conclusion:** Salbutamol exposure in dogs causes rapid onset of clinical signs in most cases, however fatalities are very rare. Treatment is aimed at correcting tachycardia and hypokalaemia.

## Reference

- [1] Mackenzie SD, Blois S, Hayes G, et al. Oral thermal injury associated with puncture of a salbutamol metered-dose inhaler in a dog. *J Vet Emerg Crit Care (San Antonio).* 2012;22:494–497.

## 345. Venlafaxine overdose in dogs: what are the risk factors associated with clinical signs?

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**Objective:** Venlafaxine is a selective serotonin reuptake inhibitor with no indication in dogs. In humans overdose causes vomiting, central nervous system (CNS) depression, electrocardiogram (ECG) changes, hypotension and seizures. The objective was to analyse the prevalence and risk factors associated with clinical signs in canine cases of venlafaxine ingestion. **Methods:** Retrospective analysis of all canine venlafaxine exposures (with outcome) reported to the Veterinary Poisons Information Service (VPIS). Asymptomatic and symptomatic populations were compared with regards to dose (one tailed t-test), age and time since ingestion (two tailed t-test), and gender (Fisher's exact test). **Results:** Of 67 cases; 40 dogs (59.7%) remained asymptomatic and 27 (40.3%) developed signs, including one that died and another that was euthanized (7.4%). Weak evidence of a difference in dose between the two groups was observed ( $p = 0.054$ ,  $n = 49$ ) and dose ingested was generally higher in symptomatic (11.5–1500 mg/kg, 37.5 mg/kg median) versus asymptomatic cases (1.3 to 168 mg/kg, 11.63 mg/kg median). Symptomatic cases presented later than asymptomatic cases with strong evidence observed for the association ( $p = 0.001$ ,  $n = 49$ ). However, of the 19 asymptomatic dogs within the dose range of symptomatic counterparts, eight received no treatment. Four of these 8 had ingested extended release preparations. Extended release preparations in symptomatic dogs were associated with higher doses and milder signs, except one dog that died (after 30–180 mg/kg). If extended release preparations were excluded stronger but still weak evidence of an association between dose and present of signs was observed ( $p = 0.04$ ,  $n = 36$ ) but this was limited by small sample size and under reporting of preparation type. There was no evidence of an association between age ( $p = 0.59$ ,  $n = 56$ ) nor gender ( $p = 0.78$ ,  $n = 56$ ) and no breed suggestive trends were observed. Signs were consistent with human poisoning except vomiting was rare 2/27 (7.4%) and associated with higher doses (346.2–1500 mg/kg). Seizures were seen in one dog which died. Tachycardia was observed at higher doses (72.5–100 mg/kg,

$n=3$ ). Neurological signs were common 26/27 (96.3%). Time to recovery ranged from 8–24 hours (average 17 hours,  $n=4$ ). **Conclusion:** Gender, age and breed are unlikely to affect venlafaxine toxicity in dogs. Dose is weakly associated with signs. When extended release preparations are excluded a stronger association is seen consistent with symptomatic extended release cases requiring less treatment at higher doses. Early presentation was associated with reduced incidence of clinical signs which, when observed, were consistent with those seen in human poisoning except vomiting and convulsions.

### 346. Ethylene glycol poisoning in cats: what are the prognostic indicators?

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**Objective:** Exposure to ethylene glycol (EG), a common component of antifreeze, is associated with very poor prognosis in cats. Exposure causes renal failure which is reversible with haemodialysis support, but this is impractical and uncommon in veterinary practice. The objective was to analyse the prevalence and risk factors associated with clinical signs in suspected EG exposure in cats. **Methods:** Retrospective analysis of suspected EG exposure in cats (with outcome) reported to the VPIS between December 1996 to February 2014. **Results:** There were 240 cases; 6 cats (2.6%) remained asymptomatic and 234 developed signs (97.5%) including 163 (69.7%) which were euthanised, 42 that died (17.9%), 24 that recovered (10.3%) and 5 with on-going signs at the time of follow up (2.1%). Most enquiries were made between October and March (153/240, 64%) peaking in December (32/240, 13%). Enquiries were greatest in male cats (95/150, 63.3%) compared to 55/150 (36.7%) females (90/240 [37.5%] had unspecified gender) and in cats aged 1–3 years 97/205 (47.3%) peaking in 2–3 year olds 40/205 (19.5%) (35/240 [14.6%] had unspecified age). The most common signs were ataxia (83/234, 35.5%), lethargy (78/234, 33.3%), vomiting (73/234, 31.2%) and collapse (73/234, 31.2%). The commonest biochemical abnormalities reported included azotaemia (113/234, 48.3%), hypocalcaemia (82/234, 35%) and hyperglycaemia (47/234, 20.1%). Oxaluria was identified in 32 cases although it was unclear if urinalysis was assessed in every case. Intravenous fluid therapy was administered in most cases (188/240, 78.3%) and ethanol in 66/240 (27.5%). Of those that received the ethanol antidote 49 died and 17 survived. Of those that survived with time to treatment reported ethanol was started within an average of 5.75 hours (median 1.5 hours,  $n=10$ ) compared to those that died or were euthanized receiving ethanol therapy (21.4 hours average, 24 hours median,  $n=17$ ). Reasons for euthanasia included poor prognosis (53/163, 32.5%) no response to treatment (26/163, 16%), worsening azotaemia (13/163, 8%), development of anuria (4/163, 2.5%), uncontrolled seizures (3/163, 1.8%) and not specified (64/163, 39.3%). Seizures occurred in 18/42 (42.9%) in those that died versus 2/24 (8.3%) that recovered. **Conclusion:** EG exposure is commonest in younger cats and in male cats and in winter months. Biochemical abnormalities such as hypocalcaemia, azotaemia and hyperglycaemia can aid diagnosis, however, prognosis is very poor particularly in cats with seizures. Antidotal therapy is only useful if started in the first few hours after exposure.

### 347. Oral exposure to fentanyl transdermal patches in dogs

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**Objective:** To determine the clinical signs and outcome in dogs after oral exposure to transdermal fentanyl patches. Even used patches contain a significant quantity of fentanyl and pose a risk. **Methods:** Retrospective analysis of cases of fentanyl transdermal patch intoxication in dogs reported to the VPIS between 2002 and September 2015. **Results:** There were 52 cases; ingestion was the most common route of exposure (57.7%,  $n=30$ ), followed by buccal where the patch was chewed but not swallowed (42.3%,  $n=22$ ). Six dogs remained asymptomatic. In 12 symptomatic dogs the patches had been used (9 patches were chewed and 3 ingested). Two cases involved the dogs just licking the area where the patch had been applied on the owner; one was asymptomatic and the other dog developed signs. Onset of effects ranged between 5 minutes and 5 hours. Of the 46 symptomatic dogs, 25 (54.3%) had neurological, 20 (43.5%) gastrointestinal, 20 (43.5%) cardiovascular, 7 (15.2%) respiratory signs and 2 (4.3%) biochemical changes. Hypersalivation (34.8%,  $n=16$ ) and bradycardia (30.4%,  $n=14$ ) were the most common signs. Other signs included pale mucous membranes ( $n=6$ ), ataxia ( $n=13$ ), hypothermia ( $n=3$ ), drowsiness ( $n=13$ ), hypoventilation ( $n=1$ ), panting ( $n=1$ ), collapse ( $n=12$ ) and coma ( $n=1$ ). Intravenous fluids 32.6% ( $n=15$ ) and activated charcoal 26.1% ( $n=12$ ) were the most frequent treatments administered. Naloxone was used in 19.6% ( $n=9$ ) of dogs with central nervous system and respiratory depression. Surgery to remove the patch was used in 8.7% ( $n=4$ ) instances. All 46 symptomatic dogs recovered fully. Time to recovery was recorded for 43.4% ( $n=20$ ) cases and varied from 1 hour to 2 days. **Conclusion:** Exposure to fentanyl transdermal patches can result in gastrointestinal, neurological, cardiovascular, biochemical and respiratory signs in dogs. In this series, neurological signs (54.3%) dominated despite the most commonly observed individual sign being hypersalivation. The overall picture is that of classic opioid poisoning with gastrointestinal signs and central nervous system and respiratory depression. There was a slight difference in the number of asymptomatic cases between buccal and ingestion exposure (9.9% versus 13.3%), suggesting ingestion is more likely to result in toxic effects compared to chewing the patch. Outcome is very good in dogs that have chewed or eaten fentanyl patches.

### 349. Racial disparities in the treatment of acute overdose in the emergency department

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**Objective:** Racial disparities continue to exist in many disciplines of medicine extending to care in the Emergency Department (ED). A disparity can be defined as a difference in the quality of healthcare due to environment, access to care, health status, or particular health outcomes.[1] We hypothesized that Blacks would

be less likely to receive treatment with activated charcoal or antidotes when presenting to the ED for acute drug overdose. **Methods:** We completed a secondary analysis of a prospective cohort of 3242 cases of patients presenting to 2 urban tertiary care hospitals with suspected acute overdose between 2009 and 2014. Categorical variables were analyzed with a chi-squared test with 2-sided  $p$  values and 5% alpha. Odds ratios (OR) were calculated with 95% CI. Assuming a baseline rate of 25% and  $\alpha = 0.05$ , we had >80% power to detect an 18% difference in the rate of antidote administration. **Results:** We screened 3242 patients, of those, 2664 were included and 410 were excluded due to alternate diagnosis ( $n = 93$ ), lack of data ( $n = 188$ ) or pediatric age ( $n = 53$ ). Mean age was 41.5 years and 55% were men. Overall there were Blacks 21.8% ( $n = 580$ ), Whites 33.67% ( $n = 897$ ), Asians 6.9% ( $n = 183$ ), other 6.9% ( $n = 185$ ), and Hispanics 30.4% ( $n = 811$ ). There were no cultural differences in poisonings and there were no associations between race and type of drug overdose. Overall 219 cases were treated with activated charcoal, either single or multi-dose, and 523 people were treated with an antidote (naloxone [ $n = 257$ ], N-acetylcysteine intravenous or oral [ $n = 136$ ], calcium [ $n = 101$ ], sodium bicarbonate [ $n = 91$ ], glucagon [ $n = 39$ ], octreotide [ $n = 29$ ], digoxin immune Fab [ $n = 10$ ], high dose insulin therapy [ $n = 6$ ,

physostigmine [ $n = 6$ ], fomepizole [ $n = 5$ ], dantrolene [ $n = 2$ ], flumazenil [ $n = 2$ ], or intravenous lipids [ $n = 1$ ]). Results of the analysis indicated that Blacks were less likely to receive activated charcoal, either one dose or multi-dose (Black 16.4%, 83.56% non-Black,  $p = 0.04$ , OR 0.687, 95% CI 0.48–0.99) and were much less likely to receive any antidote at presentation (Black 14.1%, non-Black 85.9%,  $p = 0.000001$ , OR 0.533, 95% CI 0.41–0.69). **Conclusion:** Blacks are significantly less likely to receive either activated charcoal or any antidotes when presenting to the ED for acute drug overdose. We did not assess whether those who did not receive antidotes had unmet clinical indications, which is a limitation. Further studies are needed to determine national prevalence and how race plays a role in management of acute overdose.

## Reference

- [1] Carter-Pokras O, Baquet C. What is a "health disparity"? Public Health Rep. 2002;117:426–434.